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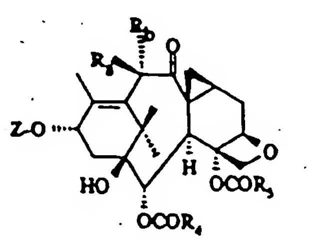
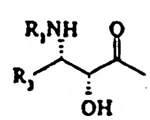
As printed

(54) Title: NEW TAXOIDS, PREPARATION THEREOF AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM

(54) Titre: NOUVEAUX TAXOIDES, LEUR PREPARATION ET LES COMPOSITIONS PHARMACEUTIQUES QUI LES CONTIENNENT

(57) Abstract


(I)


(II)

New taxoids having general formula (I), (II) preparation thereof and pharmaceutical compositions containing them. In general formula (I): R_a is hydrogen, hydroxy, alkoxy, acyloxy, alkoxyacetoxy, and R_b is hydrogen or R_a and R_b form together with the carbon atom to which they are linked a ketone function, Z is a hydrogen atom or a radical having general formula (II) wherein R_1 is an optionally substituted benzoyl radical, a thenyl or furoyl radical or a radical R_2-O-CO- wherein R_2 is an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, bicycloalkyl, optionally substituted phenyl or heterocyclyl radical; R_3 is an alkyl, alkenyl, alkynyl, cycloalkyl, phenyl, naphtyl or heterocyclic aromatic radical, and R_4 and R_5, similar or different, represent an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, bicycloalkyl, aryl or heterocyclyl radical, with the condition that R_5 does not represent a methyl radical. The new products having general formula (I) wherein Z is a radical having general formula (II) have remarkable antitumoral and antileukaemic properties.

(57) Abrégé

Nouveaux taxoïdes de formules générales (I), (II), leur préparation et les compositions pharmaceutiques qui les contiennent. Dans la formule générale (I): R_a représente hydrogène, hydroxy, alcoxy, acyloxy, alcoxyacétoxy et R_b représente hydrogène ou bien R_a et R_b forment ensemble avec l'atome de carbone auquel ils sont liés une fonction cétone; Z représente un atome d'hydrogène ou un radical de formule générale (II) dans laquelle R_1 représente un radical benzoyle éventuellement substitué, thénoyle ou furoyle ou un radical R_2-O-CO- dans lequel R_2 représente un radical alcoyle, alcényle, alcynyle, cycloalcoyle, cycloalcényle, bicycloalcoyle, phényle éventuellement substitué ou hétérocyclyle; R_3 représente un radical alcoyle, alcényle, alcynyle, cycloalcoyle, phényle, naphtyle ou hétérocyclique aromatique; et R_4 et R_5, identiques ou différents, représentent un radical alcoyle, alcényle, alcynyle, [redacted] sente un radical de formule générale (II) présen[redacted]

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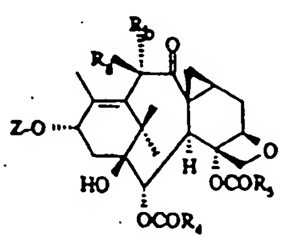
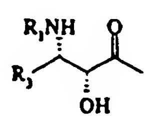

(I)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New taxoids having general formula (I), (II) preparation thereof and pharmaceutical compositions containing them. In general formula (I): R_a is hydrogen, hydroxy, alkoxy, acyloxy, alkoxyacetoxy, and R_b is hydrogen or R_a and R_b form together with the carbon atom to which they are linked a ketone function, Z is a hydrogen atom or a radical having general formula (II) wherein R_1 is an optionally substituted benzoyl radical, a thenoyl or furoyl radical or a radical R_2-O-CO- wherein R_2 is an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, bicycloalkyl, optionally substituted phenyl or heterocyclyl radical; R_3 is an alkyl, alkenyl, alkynyl, cycloalkyl, phenyl, naphthyl or heterocyclic aromatic radical, and R_4 and R_5, similar or different, represent an alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, bicycloalkyl, aryl or heterocyclyl radical, with the condition that R_5 does not represent a methyl radical. The new products having general formula (I) wherein Z is a radical having general formula (II) have remarkable antitumoral and antileukaemic properties.

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Nouveaux taxoïdes de formules générales (I), (II), leur préparation et les compositions pharmaceutiques qui les contiennent. Dans la formule générale (I): R_a représente hydrogène, hydroxy, alcoxy, acyloxy, alcoxyacétoxy et R_b représente hydrogène ou bien R_a et R_b forment ensemble avec l'atome de carbone auquel ils sont liés une fonction cétone; Z représente un atome d'hydrogène ou un radical de formule générale (II) dans laquelle R_1 représente un radical benzoyle éventuellement substitué, thénoyle ou furoyle ou un radical R_2-O-CO- dans lequel R_2 représente un radical alcoyle, alcényle, alcynyle, cycloalcoyle, cycloalcényle, bicycloalcoyle, phényle éventuellement substitué ou hétérocyclyle; R_3 représente un radical alcoyle, alcényle, alcynyle, cycloalcoyle, phényle, naphtyle ou hétérocyclique aromatique; et R_4 et R_5, identiques ou différents, représentent un radical alcoyle, alcényle, alcynyle, cycloalcoyle, cycloalcényle, bicycloalcoyle, aryle, ou hétérocyclyle, R_5 ne pouvant pas représenter un radical méthyle. Les nouveaux produits de formule générale (I) dans laquelle Z représente un radical de formule générale (II) présentent des propriétés antitumorales et antileucémiques remarquables.

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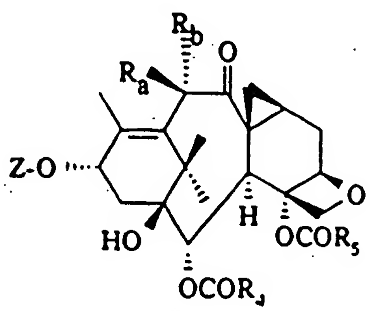
NOVEL TAXOIDS, THEIR PREPARATION AND THE PHARMACEUTICAL COMPOSITIONS WHICH CONTAIN THEM

The present invention relates to novel taxoids of general formula:

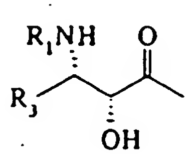


(I)

in which:

R_a represents a hydrogen atom or a hydroxyl radical, an alkoxy radical containing 1 to 4 carbon atoms, an acyloxy radical containing 1 to 4 carbon atoms or an alkoxyacetoxy radical in which the alkyl part contains 1 to 4 carbon atoms and R_b represents a hydrogen atom, or alternatively R_a and R_b form, together with the carbon atom to which they are attached, a ketone function,

Z represents a hydrogen atom or a radical of general formula:



(II)

in which:

R_1 represents a benzoyl radical optionally substituted with one or more atoms or radicals, which may be identical or different, chosen from halogen atoms and alkyl radicals containing 1 to 4 carbon atoms, alkoxy radicals containing 1 to 4 carbon atoms, trifluoromethyl, thenoyl and furoyl radicals, or a radical R_2-O-CO- in which R_2 represents:

- an alkyl radical containing 1 to 8 carbon atoms, an alkenyl radical containing 2 to 8 carbon atoms, an alkynyl radical containing 3 to 8 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a cycloalkenyl radical containing 4 to 6 carbon atoms, or a bicycloalkyl radical containing 7 to 10 carbon atoms, these radicals optionally being substituted with one or more substituents chosen from halogen atoms and hydroxyl radicals, alkoxy radicals containing 1 to 4 carbon atoms, dialkylamino radicals in which each alkyl part contains 1 to 4 carbon atoms, piperidino and morpholino radicals, 1-piperazinyl radicals (optionally substituted at -4 with an alkyl radical containing 1 to 4 carbon atoms or with a phenylalkyl radical in which the alkyl part contains 1 to 4 carbon atoms), cycloalkyl radicals containing 3 to 6 carbon atoms, cycloalkenyl radicals containing 4 to 6 carbon atoms, phenyl radicals (optionally substituted with one or more atoms or radicals chosen from halogen atoms and alkyl radicals containing 1 to 4 carbon atoms or alkoxy radicals containing 1 to 4 carbon atoms), cyano or

carboxyl radicals and alkoxycarbonyl radicals in which the alkyl part contains 1 to 4 carbon atoms,

- a phenyl or α- or β-napthyl radical which is optionally substituted with one or more atoms or radicals chosen from halogen atoms and alkyl radicals containing 1 to 4 carbon atoms or alkoxy radicals containing 1 to 4 carbon atoms or a 5-membered aromatic heterocyclic radical preferably chosen from furyl and thienyl radicals,

- or a saturated heterocyclic radical containing 4 to 6 carbon atoms optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms,

R_3 represents a straight or branched alkyl radical containing 1 to 8 carbon atoms, a straight or branched alkenyl radical containing 2 to 8 carbon atoms, a straight or branched alkynyl radical containing 2 to 8 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, or a phenyl or α- or β-naphthyl radical which is optionally substituted with one or more atoms or radicals chosen from halogen atoms and alkyl, alkenyl, alkynyl, aryl, aralkyl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxyalkyl, mercapto, formyl, acyl, acylamino, aroylamino, alkoxycarbonylamino, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, cyano, nitro and trifluoromethyl radicals, or a 5-membered aromatic heterocycle containing one or more hetero atoms, which may be

identical or different, chosen from nitrogen, oxygen and sulphur atoms and optionally substituted with one or more substituents, which may be identical or different, chosen from halogen atoms, and alkyl, aryl, amino, alkylamino, dialkylamino, alkoxycarbonylamino, acyl, arylcarbonyl, cyano, carboxyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl and alkoxycarbonyl radicals, it being understood that, in the substituents of the phenyl, α- or β-naphthyl and aromatic heterocyclic radicals, the alkyl radicals and the alkyl portions of the other radicals contain 1 to 4 carbon atoms and that the alkenyl and alkynyl radicals contain 2 to 8 carbon atoms and that the aryl radicals are phenyl or α- or β-naphthyl radicals, and

R_4 and R_5, which may be identical or different, represent

- a straight or branched alkyl radical containing 1 to 8 carbon atoms, a straight or branched alkenyl radical containing 2 to 8 carbon atoms, a straight or branched alkynyl radical containing 2 to 8 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a cycloalkenyl radical containing 4 to 6 carbon atoms or a bicycloalkyl radical containing 7 to 11 carbon atoms, these radicals optionally being substituted with one or more substituents chosen from halogen atoms and hydroxyl radicals, alkyloxy radicals containing 1 to 4 carbon atoms, dialkylamino radicals in which alkyl part contains 1 to 4 carbon atoms, piperidino and morpholino

radicals, 1-piperazinyl radicals (optionally substituted at -4 with an alkyl radical containing 1 to 4 carbon atoms or with a phenylalkyl radical in which the alkyl part contains 1 to 4 carbon atoms), cycloalkyl radicals containing 3 to 6 carbon atoms, cycloalkenyl radicals containing 4 to 6 carbon atoms, phenyl radicals which are optionally substituted, cyano and carboxyl radicals and alkyloxycarbonyl radicals in which the alkyl part contains 1 to 4 carbon atoms,

- or an aryl radical optionally substituted with one or more atoms or radicals chosen from halogen atoms and alkyl, alkenyl, alkynyl, aryl, aralkyl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxyalkyl, mercapto, formyl, acyl, acylamino, aroylamino, alkoxycarbonylamino, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, cyano, nitro, azido, trifluoromethyl and trifluoromethoxy radicals,

or a 4- to 6-membered saturated or unsaturated heterocyclic radical optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms,

it being understood that R_5 cannot represent a methyl radical,

it being understood that the cycloalkyl, cycloalkenyl and bicycloalkyl radicals may optionally be substituted with one or more alkyl radicals containing 1 to 4 carbon atoms.

The aryl radicals which may be represented by

R_3, R_4 and/or R_5 are preferably phenyl or α- or β-naphthyl radicals optionally substituted with one or more atoms or radicals chosen from halogen atoms (fluorine, chlorine, brominc or iodine) and alkyl, alkenyl, alkynyl, aryl, arylalkyl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxyalkyl, mercapto, formyl, acyl, acylamino, aroylamino, alkoxycarbonylamino, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, carbamoyl, dialkylcarbamoyl, cyano, nitro, azido, trifluoromethyl and trifluoromethoxy radicals, it being understood that the alkyl radicals and the alkyl portions of the other radicals contain 1 to 4 carbon atoms, that the alkenyl and alkynyl radicals contain 2 to 8 carbon atoms and that the aryl radicals are phenyl or α- or β-naphthyl radicals, and that the radical R_5 cannot represent a methyl radical.

The heterocyclic radicals which may be represented by R_3, R_4 and/or R_5 are preferably 5-membered aromatic heterocyclic radicals containing one or more atoms, which may be identical or different, chosen from nitrogen, oxygen and sulphur atoms, optionally substituted with one or more substituents, which may be identical or different, chosen from halogen atoms (fluorine, chlorine, bromine or iodine) and alkyl radicals containing 1 to 4 carbon atoms, aryl radicals containing 6 to 10 carbon atoms, alkoxy radicals containing 1 to 4 carbon atoms, aryloxy

radicals containing 6 to 10 carbon atoms, amino radicals, alkylamino radicals containing 1 to 4 carbon atoms, dialkylamino radicals in which each alkyl part contains 1 to 4 carbon atoms, acylamino radicals in which the acyl part contains 1 to 4 carbon atoms, alkoxycarbonylamino radicals containing 1 to 4 carbon atoms, acyl radicals containing 1 to 4 carbon atoms, arylcarbonyl radicals in which the aryl part contains 6 to 10 carbon atoms, cyano, carboxyl and carbamoyl radicals, alkylcarbamoyl radicals in which the alkyl part contains 1 to 4 carbon atoms, dialkylcarbamoyl radicals in which each alkyl part contains 1 to 4 carbon atoms, and alkoxycarbonyl radicals in which the alkoxy part contains 1 to 4 carbon atoms.

The present invention more particularly relates to the products of general formula (I) in which R_a represents a hydroxyl radical, an alkoxy radical containing 1 to 4 carbon atoms, an acyloxy radical containing 1 to 4 carbon atoms or an alkoxyacetoxy radical in which the alkyl part contains 1 to 4 carbon atoms and R_b represents a hydrogen atom, Z represents a hydrogen atom or a radical of general formula (II) in which R_1 represents a benzoyl radical or a radical R_2-O-CO- in which R_2 represents a tert-butyl radical, and R_3 represents an alkyl radical containing 1 to 6 carbon atoms, an alkenyl radical containing 2 to 6 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a phenyl radical optionally substituted with one

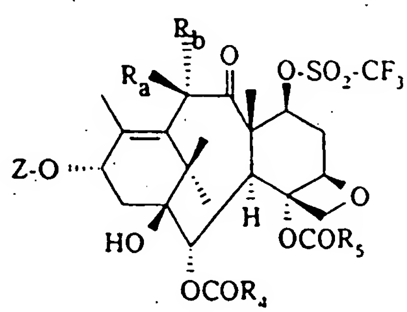
or more atoms or radicals, which may be identical or different, chosen from halogen atoms (fluorine or chlorine) and alkyl (methyl), alkoxy (methoxy), dialkylamino (dimethylamino), acylamino (acetylamino), alkoxycarbonylamino (tert-butoxycarbonylamino) or trifluoromethyl radicals or a 2- or 3-furyl, 2- or 3-thienyl or 2-, 4- or 5-thiazolyl radical, and R_4 represents a phenyl radical which is optionally substituted with one or more atoms or radicals, which may be identical or different, chosen from halogen atoms and alkyl, alkoxy, amino, alkylamino, dialkylamino, acylamino, alkoxycarbonylamino, azido, trifluoromethyl and trifluoromethoxy radicals, or a 2- or 3-thienyl or 2- or 3-furyl radical, and R_5 represents an optionally substituted alkyl radical containing 1 to 4 carbon atoms, it being understood that R_5 cannot represent a methyl radical.

Even more particularly, the present invention relates to the products of general formula (I) in which R_a represents a hydrogen atom or a hydroxyl or acetyloxy or methoxyacetoxy radical and R_b represents a hydrogen atom, Z represents a hydrogen atom or a radical of the general formula (II) in which R_1 represents a benzoyl radical or a radical R_2-O-CO- in which R_2 represents a tert-butyl radical, and R_3 represents an isobutyl, isobutenyl, butenyl, cyclohexyl, phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-thiazolyl, 4-thiazolyl or 5-thiazolyl radical, and R_4 represents a phenyl

radical which is optionally substituted with a halogen atom, and R_5 represents an alkyl radical containing 2 to 4 carbon atoms.

The products of general formula (I) in which Z represents a radical of general formula (II) have noteworthy antitumour and antileukaemia properties.

According to the invention, the products of general formula (I), in which R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical, R_b represents a hydrogen atom, and R_4, R_5 and Z are defined as above, may be obtained by the action of an alkali metal halide (sodium chloride, sodium iodide or potassium fluoride) or an alkali metal azide (sodium azide) or a quaternary ammonium salt or an alkali metal phosphate on a product of general formula:

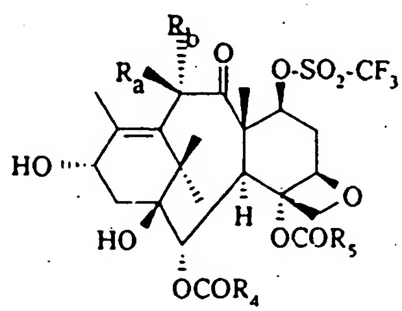


(III)

in which Z, R_4 and R_5 are defined as above, R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical or a protected hydroxyl radical, and R_b represents a hydrogen atom, followed, if necessary, by replacement of the protecting group carried by R_a by a hydrogen atom.

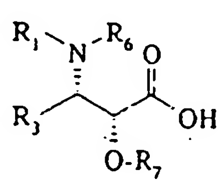
The reaction is generally carried out in an organic solvent chosen from ethers (tetrahydrofuran, diisopropyl ether or methyl tert-butyl ether) and nitriles (acetonitrile) alone or as a mixture, at a temperature between 20°C and the boiling point of the reaction mixture.

The product of general formula (III) in which Z represents a radical of general formula (II) may be obtained by esterification of a product of general formula:



(IV)

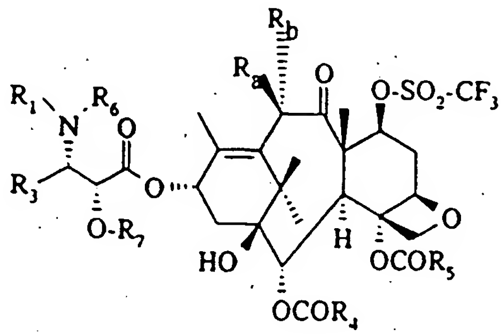
in which R_4 and R_5 are defined as above, R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical or a protected hydroxyl radical, and R_b represents a hydrogen atom, using an acid of general formula:



(V)

in which R_1 and R_3 are defined as above, or R_6 represents a hydrogen atom and R_7 represents a protecting group for the hydroxyl function, and either

R_6 and R_7 together form a 5- or 6-membered saturated heterocycle, or using a derivative of this acid, to give an ester of general formula:



(VI)

in which R_a, R_b, R_1, R_3, R_4, R_5, R_6 and R_7 are defined as above, followed by replacement of the protecting groups represented by R_7 and/or R_6 and R_7 by hydrogen atoms and optionally R_a, when it represents an acyloxy or alkoxyacetoxy radical or a protected hydroxyl radical, by a hydroxyl radical.

The esterification using an acid of general formula (V) may be carried out in the presence of a coupling agent (carbodiimide or reactive carbonate) and an activating agent (aminopyridines) in an organic solvent (ethers, esters, ketones, nitriles, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons or aromatic hydrocarbons) at a temperature between -10 and 90°C.

The esterification may also be performed using the acid of general formula (V) in anhydride form, working in the presence of an activating agent (aminopyridines) in an organic solvent (ethers, esters,

ketones, nitriles, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons or aromatic hydrocarbons) at a temperature between 0 and 90°C.

The esterification may also be performed using the acid of general formula (V) in halide form or in anhydride form with an aliphatic or aromatic acid, optionally prepared in situ, in the presence of a base (tertiary aliphatic amine), working in an organic solvent (ethers, esters, ketones, nitriles, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons or aromatic hydrocarbons) at a temperature between 0 and 80°C.

When R_a represents a protecting group for the hydroxyl function, R_a is preferably a 2,2,2-trichloroethoxycarbonyloxy radical.

Preferably, R_6 represents a hydrogen atom and R_7 represents a protecting group for the hydroxyl function, or alternatively R_6 and R_7 together form a 5- or 6-membered saturated heterocycle.

When R_6 represents a hydrogen atom, R_7 preferably represents a methoxymethyl, 1-ethoxyethyl, benzyloxymethyl, trimethylsilyl, triethylsilyl, β-trimethylsilylethoxymethyl, benzyloxycarbonyl or tetrahydropyranyl radical.

When R_6 and R_7 together form a heterocycle, this heterocycle is preferably an oxazolidine ring optionally mono-substituted or gem-disubstituted in position -2.

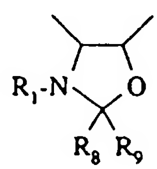
Replacement of the protecting groups R_7 and/or R_6 and R_7 by hydrogen atoms and optionally of R_8 by a hydroxyl radical may be carried out, depending on their nature, in the following way:

1) when R_6 represents a hydrogen atom and R_7 represents a protecting group for the hydroxyl function and R_8 represents an alkoxy, acyloxy or alkoxyacetoxy radical, replacement of the protecting groups by hydrogen atoms is carried out using an inorganic acid (hydrochloric acid, sulphuric acid or hydrofluoric acid) or an organic acid (acetic acid, methanesulphonic acid, trifluoromethanesulphonic acid or p-toluenesulphonic acid) used alone or as a mixture, working in an organic solvent chosen from alcohols, ethers, esters, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons, aromatic hydrocarbons and nitriles, at a temperature between -10 and 60°C,

2) When R_6 represents a hydrogen atom and R_7 represents a protecting group for the hydroxyl function and R_8 represents a 2,2,2-trichloroethoxycarbonyloxy radical, replacement of the protecting group R_7 is carried out under the conditions described above in 1) and that of R_8 is carried out by treatment using zinc, optionally combined with copper, in the presence of acetic acid at a temperature between 30 and 60°C, or using an inorganic or organic acid such as hydrochloric acid or

acetic acid dissolved in an aliphatic alcohol containing 1 to 3 carbon atoms (methanol, ethanol, propanol or isopropanol) or in an aliphatic ester (ethyl acetate, isopropyl acetate or n-butyl acetate) in the presence of zinc which is optionally combined with copper,

3) when R_6 and R_7 together form a 5- or 6-membered saturated heterocycle and more particularly an oxazolidine ring of general formula:

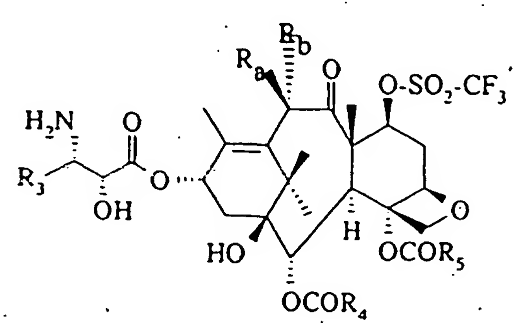


(VII)

in which R_1 is defined as above, R_8 and R_9, which may be identical or different, represent a hydrogen atom or an alkyl radical containing 1 to 4 carbon atoms, or an aralkyl radical in which the alkyl part contains 1 to 4 carbon atoms and the aryl part preferably represents a phenyl radical optionally substituted with one or more alkoxy radicals containing 1 to 4 carbon atoms, or an aryl radical preferably representing a phenyl radical optionally substituted with one or more alkoxy radicals containing 1 to 4 carbon atoms, or alternatively R_8 represents an alkoxy radical containing 1 to 4 carbon atoms or a trihalomethyl radical such as trichloromethyl or a phenyl radical substituted with a trihalomethyl radical such as trichloromethyl and R_9

represents a hydrogen atom, or alternatively R_8 and R_9 form, together with the carbon atom to which they are attached, a 4- to 7-membered ring, and R_a represents an acyloxy or alkoxyacetoxy or 2,2,2-trichloroethoxycarbonyloxy radical, replacement of the protecting group formed by R_6 and R_7 by hydrogen atoms and of R_a by a hydroxyl radical may be carried out, depending on the meanings of R_a, R_1, R_8 and R_9, in the following way:

a) when R_1 represents a tert-butoxycarbonyl radical, R_8 and R_9, which may be identical or different, represent an alkyl radical or an aralkyl (benzyl) or aryl (phenyl) radical, or alternatively R_8 represents a trihalomethyl radical or phenyl radical substituted with a trihalomethyl radical, and R_9 represents a hydrogen atom, or alternatively R_8 and R_9 together form a 4- to 7-membered ring, treatment of the ester of general formula (VI) with an inorganic or organic acid, optionally in an organic solvent such as an alcohol, gives the product of general formula:



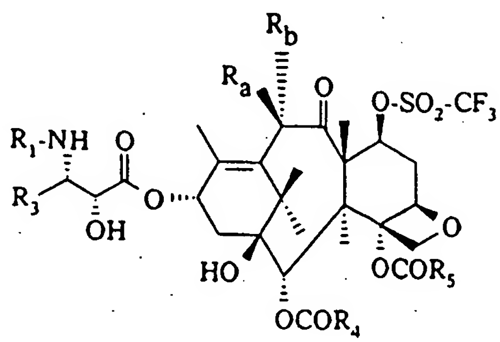
(VIII)

in which R_a, R_b, R_3, R_4 and R_5 are defined as above,

which compound is acylated using benzoyl chloride in which the phenyl ring is optionally substituted, thenoyl chloride, furoyl chloride or a product of general formula:

$$R_2\text{-O-CO-X} \qquad \text{(IX)}$$

in which R_2 is defined as above and X represents a halogen atom (fluorine or chlorine) or a residue $-O-R_2$ or $-O-CO-O-R_2$, in order to obtain a product of general formula:



(X)

in which R_a, R_b, R_1, R_3, R_4 and R_5 are defined as above, the protecting group R_a of which compound, when it represents a protected hydroxyl radical, is replaced, if necessary, by a hydroxyl radical.

Preferably, the product of general formula (VI) is treated with formic acid at a temperature in the region of 20°C.

Acylation of the product of general formula (VIII) using a benzoyl chloride in which the phenyl radical is optionally substituted, thenoyl chloride or furoyl chloride or a product of general formula (IX) is preferably carried out in an inert organic solvent

chosen from esters such as ethyl acetate, isopropyl acetate or n-butyl acetate and halogenated aliphatic hydrocarbons such as dichloromethane or 1,2-dichloroethane, in the presence of an inorganic base such as sodium bicarbonate or an organic base such as triethylamine. The reaction is carried out at a temperature between 0 and 50°C, preferably in the region of 20°C.

Replacement of the protecting group of R_a, when it represents a 2,2,2-trichloroethoxycarbonyloxy radical, is preferably carried out under the conditions described above in 2),

b) when R_1 represents a benzoyl radical which is optionally substituted, a thenoyl or furoyl radical or a radical R_2O-CO- in which R_2 is defined as above, R_6 represents a hydrogen atom, an alkoxy radical containing 1 to 4 carbon atoms or a phenyl radical substituted with one or more alkoxy radicals containing 1 to 4 carbon atoms, and R_7 represents a hydrogen atom, replacement of the protecting group formed by R_6 and R_7 by hydrogen atoms is carried out in the presence of an inorganic acid (hydrochloric acid or sulphuric acid) or an organic acid (acetic acid, methanesulphonic acid, trifluoromethanesulphonic acid or p-toluenesulphonic acid) used alone or as a mixture, in a stoichiometric or catalytic amount, working in an organic solvent chosen from alcohols, ethers, esters, aliphatic hydrocarbons, halogenated aliphatic hydrocarbons and

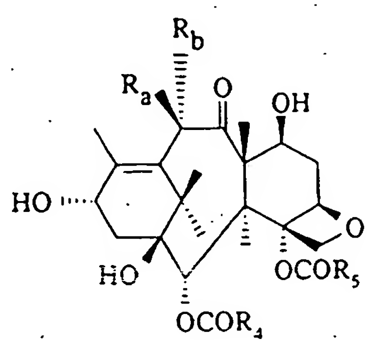
aromatic hydrocarbons, at a temperature between -10 and 60°C, preferably between 15 and 30°C, and replacement of the protecting group of R_a, when it represents a 2,2,2-trichloroethoxycarbonyloxy radical, by a hydrogen atom is carried out under the conditions described above in 2).

4) when R_a represents an alkoxyacetyl radical and R_6 and R_7 are defined as in point 1) above, firstly, the protecting group R_7 is replaced by a hydrogen atom, working under the acidic conditions described in point 1) above, optionally followed by replacement of R_a by a hydroxyl radical, by treatment in an alkaline medium or by the action of a zinc halide under conditions which do not affect the rest of the molecule. The alkaline treatment is generally carried out by the action of ammonia in an aqueous-alcoholic medium at a temperature in the region of 20°C. The treatment with a zinc halide, preferably zinc iodide, is generally carried out in methanol at a temperature in the region of 20°C.

5) when R_a represents an alkoxyacetoxy radical and R_6 and R_7 are defined as in point 2-a) above, the radical R_a is replaced by a hydroxyl radical by treatment in alkaline medium or by treatment using a zinc halide under the conditions described in point 3) above, followed by treatment of the product of general formula (VI) obtained under the deprotection and acylation conditions described in point 2-a) above.

6) when R_a represents an alkoxyacetoxy radical and R_6 and R_7 are defined as in point 2-b) above, the radical R_a is replaced by a hydroxyl radical by treatment in an alkaline medium or by treatment using a zinc halide under the conditions described in point 3) above, followed by treatment of the product obtained under the conditions described in point 2-b) above.

According to the invention, the products of general formula (III) in which R_4 and R_5 are defined as above, R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical, and R_b represents a hydrogen atom, or alternatively R_a and R_b form, together with the carbon atom to which they are attached, a ketone function, and Z represents a hydrogen atom, may be obtained by the action of a trifluoromethanesulphonic acid derivative, such as the anhydride or the N-phenyltrifluoromethanesulphonimide, on a product of general formula:



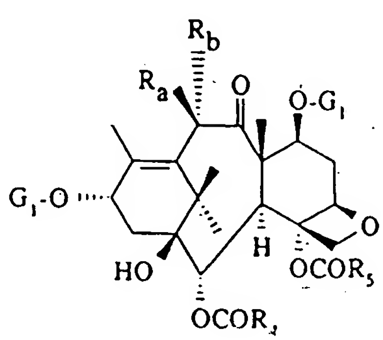
(XI)

in which R_a, R_b, R_4 and R_5 are defined as above.

The reaction is generally carried out in an inert organic solvent (optionally halogenated aliphatic

hydrocarbons, or aromatic hydrocarbons) in the presence of an organic base such as an aliphatic tertiary amine (triethylamine) or pyridine, at a temperature between -50 and +20°C.

The products of general formula (XI) in which R_4 and R_5 are defined as above, R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical or a protected hydroxyl radical, and R_b represents a hydrogen atom, may be obtained by the action of hydrofluoric acid or trifluoroacetic acid in a basic organic solvent, such as pyridine optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms, or triethylamine optionally in combination with an inert organic solvent such as methylenechloride or acetonitrile or tetrahydrofuran, at a temperature between 20 and 80°C, on a product of general formula:



(XII)

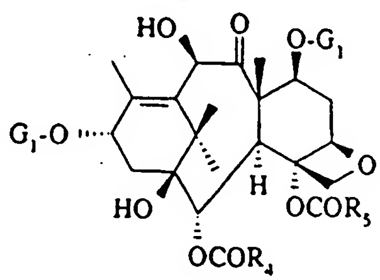
in which R_4 and R_5 are defined as above, R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical or a protected hydroxyl radical, R_b represents a hydrogen atom, and the symbols G_1, which are identical,

represent a trialkylsilyl radical.

The product of general formula (XII) may be obtained by the action of a product of general formula:

$$R\text{-}Y \qquad (XIII)$$

in which R represents an alkyl, alkanoyl or alkoxyacetyl radical or a protecting group for the hydroxyl function and Y represents a halogen atom, on a product of general formula:



(XIV)

in which R_4, R_5 and G_1 are defined as above.

When R represents an alkyl or alkoxyacetyl radical, it is particularly advantageous to work in a basic organic solvent such as pyridine or in an inert organic solvent such as methylene chloride, chloroform or 1,2-dichloroethane, in the presence of a tertiary amine such as triethylamine or pyridine, at a temperature in the region of 0°C.

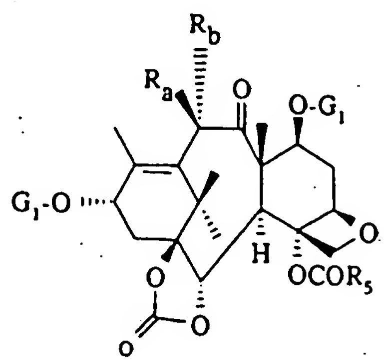
When R represents an alkyl radical, it is particularly advantageous to metallate the hydroxyl function at -10 beforehand using an alkali metal hydride (sodium hydride) or a metal alkylide (butyllithium).

The product of general formula (XIV) and,

optionally, the product of general formula (XII) may be obtained by the action of an organometallic derivative of general formula:

R_4-M (XV)

in which R_4 is defined as above and M represents a metal atom, preferably a lithium or magnesium atom, on a product of general formula:

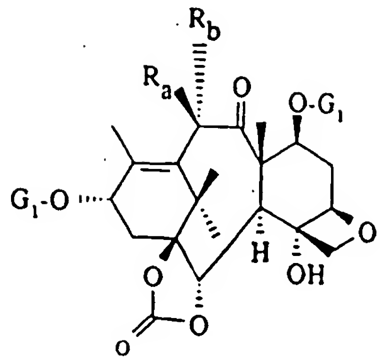


(XVI)

in which R_a, R_b, R_5 and G_1 are defined as above.

The reaction is generally carried out in an organic solvent such as an ether (tetrahydrofuran) at a temperature below -50°C, preferably in the region of -78°C.

The product of general formula (XVI) may be obtained by esterification of a product of general formula:



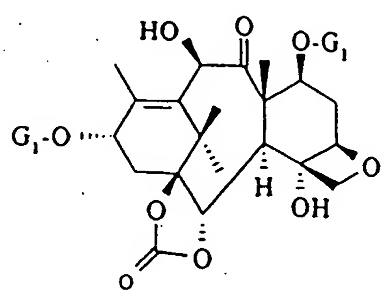
(XVII)

in which R_a, R_b and G_1 are defined as above, using an acid of general formula:

R_5-COOH (XVIII)

in which R_5 is defined as above, or using a derivative of this acid such as a halide or an anhydride, in the presence of a coupling agent or of an inorganic or organic base.

The product of general formula (XVII) may be obtained by the action of a product of general formula (XIII) on a product of general formula:

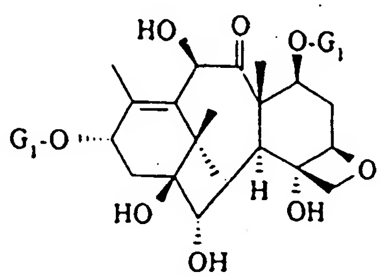


(XIX)

in which G_1 is defined as above, under the conditions described above for the action of a product of general formula (XIII) on a product of general formula (XIV).

The product of general formula (XIX) may be

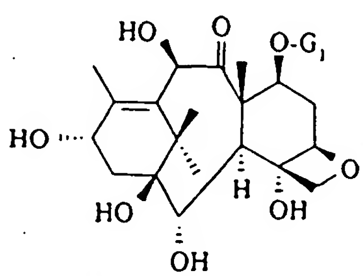
prepared by the action of phosgene, or one of the derivatives thereof such as triphosgene, on a product of general formula:



(XX)

in which G_1 is defined as above, working in a basic organic solvent such as pyridine, at a temperature below -50°C, preferably in the region of -78°C.

The product of general formula (XX) may be prepared by the action of a halotrialkylsilane on a product of general formula:



(XXI)

in which G_1 is defined as above, working in a basic organic solvent.

The product of general formula (XXI) may be prepared under the conditions described by D.G.I. Kingston et al., Journal of Nat. Prod., 56, 884 (1993).

The product of general formula (I) in which R_a and R_b each represent a hydrogen atom may be obtained by

electrolytic reduction of a product of general formula (I) in which R_a represents a hydroxyl radical or an acyloxy or alkoxyacetoxy radical or under the conditions described in International Application PCT WO 93/06093.

The products of general formula (I) in which R_a and R_b form, together with the carbon atom to which they are attached, a ketone function may be obtained by oxidation of a product of general formula (I) in which R_a represents a hydroxyl radical and R_b represents a hydrogen atom, using, for example, pyridinium chlorochromate, pyridinium dichromate, potassium dichromate, ammonium dichromate or manganese dioxide.

The novel products of general formula (I) obtained using the processes according to the invention may be purified according to the known methods, such as crystallization or chromatography.

The products of general formula (I) in which Z represents a radical of general formula (II) have noteworthy biological properties.

In vitro, measurement of the biological activity is carried out on tubulin extracted from pig brain by the method of M.L. Shelanski et al., Proc. Natl. Acad. Sci. USA, <u>70</u>, 765-768 (1973). Study of the depolymerization of microtubules into tubulin is carried out according to the method of G. Chauvière et al., C.R. Acad. Sci., <u>293</u>, 2nd series, 501-503 (1981). In this study, the products of general formula (I) in

which Z represents a radical of general formula (II) proved to be at least as active as taxol and Taxotere.

In vivo, the products of general formula (I) in which Z represents a radical of general formula (II) proved to be active in mice grafted with melanoma B16 at doses between 1 and 10 mg/kg via the intraperitoneal route, as well as on other liquid or solid tumours.

The novel products have antitumour properties and more particularly an activity on tumours which are resistant to Taxol® or to Taxotere®. Such tumours comprise tumours of the colon which have a high expression of the mdr 1 gene (multi-drug resistance gene). Multi-drug resistance is a common term relating to the resistance of a tumour to various products having various structures and mechanisms of action. Taxoids are generally known for being highly recognized by experimental tumours such as P388/DOX, a cell line selected for its resistance to doxorubicin (DOX) which expresses mdr 1.

The examples which follow illustrate the present invention.

EXAMPLE 1

To a solution of 0.193 g of 2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S)-3-tert-butoxycarbonylamino-2-hydroxy-4-phenylpropionate in 2.5 cm^3 of acetonitrile and

0.250 cm^3 of tetrahydrofuran are successively added 0.096 g of powdered 4Å molecular sieves and 0.290 g of sodium chloride. The reaction mixture is kept stirring at a temperature in the region of 75°C for 5 hours, and then, at a temperature in the region of 20°C, 75 cm^3 of dichloromethane and 50 cm^3 of saturated aqueous sodium chloride solution are added. The organic phase is separated out after settling of the phases has taken place, washed twice with 40 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 0.150 g of a product is obtained, which is purified by chromatography on 80 g of silica (0.063-0.2 mm) contained in a column 1 cm in diameter (eluent: dichloromethane/methanol: 98/2 by volume), collecting 10 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 0.080 g of 2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-7β,8-methylene-19-nor-9-oxo-4α-propanoyloxy-11-taxen-13α-yl (2R,4S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate is obtained, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.24 (t, J = 7.5 Hz, 3H : CH_3 ethyl); 1.24 (s, 6H : CH_3); 1.27 (s, 9H : $C(CH_3)_3$) ; 1.42 (mt, 1H : H 7); 1.68 and 2.24 (2 mts, 1H each: CH_2 at 19); 1.86 (s, 1H: OH at 1); 1.86

(s, 3H : CH_3); 2.12 and 2.86 (d and dt respectively, J = 16 and 5 Hz, 1H each: CH_2 at 6); from 2.15 to 2.30 and 2.41 (mt and dd respectively, J = 16 and 9 Hz, 1H each: CH_2 at 14); 2.64 (mt, 2H: CH_2 ethyl); 3.26 (mt, 1H: OH at 2'); 3.52 (s, 3H : OCH_3); 4.07 (d, J = 7 Hz, 1H : H at 3); 4.04 and 4.33 (2d, J = 9 Hz, 1H each: CH_2 at 20); 4.22 (limiting AB, J = 16 Hz, 2H: $OCOCH_2O$); 4.62 (mt, 1H : H at 2'); 4.70 (d, J = 4 Hz, 1H : H at 5); 5.28 (md, 2H: H at 3' and CONH); 5.67 (d, J = 7 Hz, 1H : H at 2); 6.26 (broad t, J = 9 Hz, 1H : H at 13); 6.42 (s, 1H : H at 10); from 7.25 to 7.45 (mt, 5H : aromatic H at 3'); 7.52 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.62 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.16 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

2α-Benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S)-3-tert-butoxycarbonylamino-2-hydroxy-4-phenylpropionate may be prepared the following way:

A solution of 0.760 g of 2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-7β-trifluoromethanesulphonate-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate in 6.6 cm^3 of 0.1N hydrochloric ethanol solution is kept stirring at a temperature in the region of 0°C for 22 hours. The reaction medium is concentrated to dryness under reduced pressure (2.7 kPa) at 20°C. The crude

reaction material is dissolved in 80 cm^3 of dichloromethane and 80 cm^3 of saturated aqueous sodium bicarbonate solution. The organic phase is separated out after settling of the phases has taken place and then extracted with twice 50 cm^3 of dichloromethane. The organic phases are combined, washed with 50 cm^3 of distilled water and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 20°C. 0.9 g of a white foam is obtained, which is purified by chromatography on 150 g of silica (0.063-0.2 mm) contained in a column 3 cm in diameter (eluent: dichloromethane/methanol: 95/5 by volume), collecting 15 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 20°C. 0.456 g of 2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S)-3-tert-butoxycarbonylamino-2-hydroxy-4-phenylpropionate is obtained, the physical characteristics of which are as follows:

- ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.24 (s, 9H : CH_3 and CH_3 ethyl); 1.34 (s, 9H : $C(CH_3)_3$); 1.74 (s, 1H : OH at 1); 1.88 (s, 3H : CH_3); 2.05 (broad s, 3H : CH_3); 2.24 and 2.86 (2 mts, 1H each: CH_2 at 6); 2.33 (d, J = 9 Hz, 2H : CH_2 at 14); 2.68 (mt, 2H : CH_2 ethyl); 3.30 (mt, 1H : OH at 2'); 3.52 (s, 3H : OCH_3); 3.93 (mt, 1H : H at 3); 4.19 (limiting AB, J = 16 Hz,

2H : $OCOCH_2O$); 4.20 and 4.36 (2d, J = 9 Hz, 1H each: CH_2 at 20); 4.64 (broad d, J = 5.5 Hz, 1H : H at 2'); 4.86(broad d, J = 10 Hz, 1H : H at 5); 5.22 (mt, 1H : H at 3'); 5.30 (d, J = 10 Hz, 1H : CONH); 5.51 (dd, J = 10 and 7.5 Hz, 1H : H at 7); 5.75 (d, J = 7 Hz, 1H : H at 2); 6.20 (mt, 1H : H at 13); 6.71 (s, 1H : H at 10); from 7.30 to 7.45 (mt, 5H : aromatic H at 3'); 7.52 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.64 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.13 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

2α-Benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate may be prepared in the following way:

To a solution of 0.590 g of 2α-benzoyloxy-1β,13α-dihydroxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-7β-trifluoromethanesulphonyloxy-11-taxene in 10 cm^3 of anhydrous ethyl acetate are successively added 0.463 g of (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylic acid, 0.319 g of dicyclohexylcarbodiimide and 0.028 g of 4-dimethylaminopyridine. The reaction mixture is stirred for 15 hours, under an argon atmosphere, at a temperature in the region of 20°C, followed by addition of 75 cm^3 of dichloromethane and 50 cm^3 of saturated

aqueous ammonium chloride solution. The organic phase is separated out after settling of the phases has taken place, washed with twice 40 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 0.980 g of product are obtained, which is purified by chromatography on 150 g of silica (0.063-0.2 mm) contained in a column 3 cm in diameter (eluent: dichloromethane/methanol: 95/5 by volume), collecting 15 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 0.740 g of 2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate is obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 1.06 (s, 12H : CH_3 and $C(CH_3)_3$); 1.20 (s, 3H : CH_3); 1.27 (t, J = 7.5 Hz, 3H : CH_3 ethyl); 1.67 (s, 1H : OH at 1); 1.71 (s, 3H : CH_3); 1.83 (s, 3H : CH_3); from 2.00 to 2.30 and 2.83 (2 mt, 1H each : CH_2 at 6); from 2.00 to 2.30 (mt, 2H : CH_2 ethyl); 2.08 and 2.22 (2 dd, J = 16 and 9 HZ, 1H each : CH_2 at 14); 3.52 (s, 3H : OCH_3); 3.82 (s, 3H : $ArOCH_3$); 3.82 (mt, 1H : H at 3); 4.12 and 4.29 (2d, J = 9 Hz, 1H each : CH_2 at 20); 4.18 (limiting AB,

J = 16 Hz, 2H : $OCOCH_2O$); 4.51 (d, J = 5 Hz, 1H : H at 2'); 4.80 (broad d, J = 10 Hz, 1H : H5); from 5.35 to 5.45 (mt, 1H : H at 3'); 5.43 (dd, J = 10.5 and 7.5 Hz, 1H : H at 7); 5.68 (d, J = 7 Hz, 1H : H at 2); 6.01 (mt, 1H : H at 13); 6.38 (mt, 1H : H at 5'); 6.60 (s, 1H : H at 10); 6.92 (d, J = 8.5 Hz, 2H : aromatic H ortho to the OCH_3); 7.39 (d, J = 8.5 Hz, 2H : aromatic H meta to the OCH_3); from 7.30 to 7.45 (mt, 5H : aromatic H at 3'); 7.50 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.65 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.03 (d, j = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

2α-Benzoyloxy-1β,13α-dihydroxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-7β-trifluoromethanesulphonyloxy-11-taxene may be prepared in the following way:

To a solution of 0.660 g of 2α-benzoyloxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-1β,7β,13α-trihydroxy-11-taxene in 6.6 cm^3 of anhydrous dichloromethane and 0.338 cm^3 of pyridine, maintained under an argon atmosphere, and at a temperature in the region of 0°C, is added dropwise 0.354 cm^3 of trifluoromethanesulphonic anhydride. The orange-coloured solution obtained is stirred for 10 minutes at a temperature in the region of 0°C and for 30 minutes at a temperature in the region of 20°C, followed by addition of 3 cm^3 of water and 50 cm^3 of dichloromethane. The organic phase is separated out after settling of the phases has taken place, washed

with twice 40 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 0.800 g of product is obtained, which is purified by chromatography on 100 g of silica (0.063-0.2 mm) contained in a column 2 cm in diameter (eluent: dichloromethane/methanol: 95/5 by volume), collecting 15 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 0.591 g of 2α-benzoyloxy-1β,13α-dihydroxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-7β-trifluoromethanesulphonyloxy-11-taxene is obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 1.05 (s, 3H : CH_3); 1.19 (s, 3H : CH_3); 1.23 (t, J = 7.5 Hz, 3H : CH_3 ethyl); 1.62 (s, 1H : OH at 1); 1.89 (s, 3H : CH_3); 2.12 (d, J = 5 Hz, 1H : OH at 13); 2.24 and 2.90 (2 mts, 1H each : CH_2 at 6); 2.25 (s, 3H : CH_3); 2.30 (limiting AB, 2H : CH_2 at 14); 2.64 (mt, 2H : CH_2 ethyl); 3.52 (s, 3H : OCH_3); 4.02 (d, J = 7 Hz, 1H : H at 3); 4.15 and 4.35 (2d, J = 9 Hz, 1H each : CH_2 at 20); 4.20 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.85 (mt, 1H : H at 13); 4.91 (broad d, J = 10 Hz, 1H : H at 5); 5.57 (dd, J = 10 and 7 Hz, 1H : H at 7); 5.69 (d, J = 7 Hz, 1H : H at 2); 6.73 (s, 1H : H at 10); 7.50 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.63 (t, J = 7.5 Hz,

1H : $OCOC_6H_5$ para-H); 8.11 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

2α-Benzoyloxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-1β,7β,13α-trihydroxy-11-taxene may be prepared in the following way:

To a solution of 1.21 g of 2α-benzoyloxy-7β,13α-ditriethylsilyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-11-taxene in 15 cm^3 of dichloromethane are added, at a temperature in the region of 20°C, 23 cm^3 of triethylamine-hydrofluoric acid complex. The reaction mixture is stirred for 20 hours at a temperature in the region of 20°C, followed by addition of 50 cm^3 of dichloromethane and 100 cm^3 of saturated aqueous sodium hydrogen carbonate solution. The organic phase is separated out after settling of the phases has taken place, washed with twice 50 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 1.04 g of 2α-benzoyloxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-1β,7β,13α-trihydroxy-11-taxene are obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.11 (s, 6H : CH_3); 1.25 (t, J = 7.5 Hz, 3H : CH_3 ethyl); 1.65 (s, 1H : OH at 1); 1.70 (s, 3H : CH_3); 1.88 and 2.60 (2 mts, 1H each : CH_2 at 6); 2.08 (s, 3H : CH_3); 2.30

(limiting AB, 2H : CH_2 at 14); 2.39 (d, J = 4 Hz, 1H : OH at 7); ~ 63 (mt, 2H : CH_2 ethyl); 3.55 (s, 3H : OCH_3); 3.90 (d, J = 7 Hz, 1H : H at 3); 4.17 and 4.32 (2d, J = 9 Hz, 1H each : CH_2 at 20); 4.25 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.51 (mt, 1H : H at 7); 4.89 (mt, 1H : H at 13); 4.95 (broad d, J = 10 Hz, 1H : H at 5); 5.64 (d, J = 7 Hz, 1H : H at 2); 6.43 (s, 1H : H at 10); 7.48 (t, J = 8 Hz, 2H : $OCOC_6H_5$ meta-H); 7.61 (t, J = 8 Hz, 1H : $OCOC_6H_5$ para-H); 8.13 (d, J = 8 Hz, 2H : $OCOC_6H_5$ ortho-H).

2α-Benzoyloxy-7β,13α-ditriethylsilyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-11-taxene may be prepared in the following way:

To a solution of 0.900 g of 2α-benzoyloxy-1β,10β-dihydroxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-4α-propanoyloxy-11-taxene in 15 cm^3 of pyridine is added, at a temperature in the region of 0°C, 0.520 cm^3 of methoxyacetyl chloride. The reaction mixture is stirred for 2 hours at a temperature in the region of 20°C, followed by addition of 100 cm^3 of dichloromethane and 50 cm^3 of saturated aqueous ammonium chloride solution. The organic phase is separated out after settling of the phases has taken place, washed with twice 40 cm^3 of saturated aqueous ammonium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 1.3 g of product are

obtained, which product is purified by chromatgraphy on 150 g of silica (0.063-0.2 mm) contained in a column 2.5 cm in diameter (eluent: ethyl acetate/cyclohexane : 25/75 by volume), collecting 10 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 0.780 g of 2α-benzoyloxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-11-taxene is obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : from 0.50 to 0.70 (mt, 12 H : CH_2 ethyl); 0.92 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.00 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.10 (s, 3H : CH_3); 1.17 (s, 3H : CH_3); 1,29 (t, J = 7.5 Hz, 3H : CH_3 ethyl at 4); 1.61 (s, 1H : OH at 1); 1.68 (s, 3H : CH_3); 1.84 and 2.51 (2 mts, 1H each : CH_2 at 6); 2.09 and 2.21 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 2.10 (s, 3H : CH_3); 2.60 (mt, 2H : CH_2 ethyl at 4); 3.50 (s, 3H : OCH_3); 3.78 (d, J = 7 Hz, 1H : H at 3); 4.12 and 4.30 (2d, J = 9 Hz, 1H each : CH_2 at 20); 4.15 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.49 (dd, J = 11 and 7 Hz, 1H : H at 7); 4.90 (mt, 2H : H at 5 and H at 13); 5.62 (d, J = 7 Hz, 1H : H at 2); 6.52 (s, 1H : H at 10); 7.45 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H; 7.58 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.09 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

2α-Benzoyloxy-1β,10β-dihydroxy-7β,13α-

bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-4α-propanoyloxy-11-taxene may be prepared in the following way:

To a solution of 1.105 g of 1β,2α-carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-11-taxene in 50 cm^3 of tetrahydrofuran anhydride are added, at a temperature in the region of -78°C, 1.8 cm^3 of a 1M solution of phenyllithium in tetrahydrofuran. The reaction mixture is stirred for 15 minutes at a temperature in the region of -78°C, followed by addition of 10 cm^3 of saturated aqueous ammonium chloride solution. At a temperature in the region of 20°C, 20 cm^3 of saturated aqueous ammonium chloride solution and 50 cm^3 of dichloromethane are added. The organic phase is separated out after settling of the phases has taken place, washed with twice 10 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 1.3 g of product are obtained, which product is purified by chromatography on 150 g of silica (0.063-0.2 mm) contained in a column 5 cm in diameter (eluent: ethyl acetate/cyclohexane: 10/90 by volume), collecting 18 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 0.840 g of 2α-benzoyloxy-1β,10β-

dihydroxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-4α-propanoyloxy-11-taxene is obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : from 0.53 (mt, 6 H : CH_2 ethyl); 0.65 (mt, 6 H : CH_2 ethyl); 0.92 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.00 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.07 (s, 3H : CH_3); 1.14 (s, 3H = : CH_3); 1.26 (t, J = 7.5 Hz, 3H : CH_3 ethyl at 4); 1.40 (s, 1H : OH at 1); 1.71 (s, 3H : CH_3); 1.88 and 2.45 (2 mts, 1H each: CH_2 at 6); 2.00 (s, 3H : CH_3); 2.06 and 2.18 (2 dd, J = 16 and 9 Hz, 1H each: CH_2 at 14); 2.60 (q, J = 7.5 Hz, 2H : CH_2 ethyl at 4); 3.84 (d, J = 7 Hz, 1H : H at 3); 4.14 and 4.30 (2d, J = 8.5 Hz, 1H each : CH_2 at 20); 4.26 (d, J = 0.5 Hz, 1H : OH at 10); 4.40 (dd, J = 11 at 7 Hz, 1H : H at 7); 4.90 (broad d, J = 10 Hz, 1H : H at 5); 4.94 (broad t, = 9 Hz, 1H : H at 13); 5.12 (d, J = 0.5 Hz, 1H : H at 10); 5.58 (d, J = 7 Hz, 1H : H at 2); 7.45 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.60 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para H); 8.09 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

1β,2α-Carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-11-taxene may be prepared in the following way:

To a solution of 2.0 g of 1β,2α-carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-4α-hydroxy-10β-methoxyacetoxy-9-oxo-11-taxene in 90 cm^3 of dichloromethane are added 3.7 g of

4-dimethylaminopyridine and 3.64 cm^3 of propionic anhydride. The reaction medium is heated at a temperature in the region of 42°C for 8 hours. 50 cm^3 of saturated aqueous sodium chloride solution and 50 cm^3 of dichloromethane are added. The organic phase is separated out after settling of the phases has taken place, washed with twice 40 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 2.6 g of product are obtained, which product is purified by chromatography on 100 g of silica (0.063-0.2 mm) contained in a column 3 cm in diameter (eluent: ethyl acetate/cyclohexane : 5/95 by volume), collecting 12 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 1.97 g of 1β,2α-carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-11-taxene are obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): from 0.50 to 0.75 (mt, 12H : CH_2 ethyl); 0.94 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.03 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.21 (mt, 6H : CH_3 and CH_3 ethyl); 1.28 (s, 3H : CH_3); 1.75 (s, 3H : CH_3); 1.90 and 2.60 (2 mts, 1 H each: CH_2 at 6); 2.13 (s, 3H : CH_3); 2.15 and 2.38 (2 dd, J = 16 and

9 Hz, 1 H each: CH_2 at 14); 2.43 (mt, 2H : CH_2 ethyl); 3.43 (d, J = 5.5 Hz, 1H : H at 3); 3.51 (s, 3H : OCH_3); 4.18 (s, 2H : $OCOCH_2O$); 4.46 (dd, J = 11 and 7 Hz, 1H : H at 7); 4.48 and 4.65 (2d, J = 9Hz, 2H : CH_2 at 20); 4.51 (d, J = 5.5 HZ, 1 H : H at 2); 4.93 (broad d, J = 10 Hz, 1 H : H at 5); 5.02 (t, J = 9 Hz, 1 H : H at 13); 6.51 (s, 1H : H at 10).

1β,2α-Carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-4α-hydroxy-10β-methoxyacetoxy-9-oxo-11-taxene may be prepared in the following way:

To a solution of 4.12 g of 1β,2α-carbonato-4α,10β-dihydroxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-11-taxene in 80 cm^3 of pyridine are added, with stirring and at a temperature in the region of 0°C, 2 g of powdered 4Å molecular sieves and 2.86 cm^3 of methoxyacetyl chloride. The reaction mixture is stirred for 15 minutes at a temperature in the region of 0°C and the reaction medium is then allowed to warm slowly to a temperature in the region of 20°C. After stirring for 4 hours at a temperature in the region of 20°C, 50 cm^3 of saturated aqueous ammonium chloride solution and 100 cm^3 of dichloromethane are added. The organic phase is separated out after settling of the phases has taken place, washed with twice 40 cm^3 of saturated aqueous ammonium chloride solution, with twice 25 cm^3 of saturated aqueous copper sulphate solution and with twice 25 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate,

filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 5.3 g of product are obtained, which product is purified by chromatography on 200 g of silica (0.063-0.2 mm) contained in a column 4 cm in diameter (eluent: ethyl acetate/cyclohexane : 25/75 by volume), collecting 12 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 4.21 g of 1β,2α-carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-4α-hydroxy-10β-methoxyacetoxy-9-oxo-11-taxene are obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 0.59 (mt, 6H : CH_2 ethyl); 0.73 (mt, 6H : CH_2 ethyl); 0.91 (t, J = 7.5 Hz, 9 H : CH_3 ethyl); 1.02 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.15 (s, 3H : CH_3); 1.18 (s, 3H : CH_3); 1.65 (s, 3H : CH_3); 1.98 and 2.51 (2 mts, 1 H each : CH_2 at 6); 2.15 (s, 3H : CH_3); 2.54 and 2.72 (2 dd respectively, J = 16 and 9 Hz and J = 16 and 3 Hz, 1H each : CH_2 at 14); 2.93 (s, 1H : OH at 4); 3.03 (d, J = 5 Hz, 1H : H at 3); 3.51 (s, 3H : $-OCH_3$); 4.16 (mt, 1H : H at 7); 4.17 (AB, J = 18 Hz, 2H : $OCOCH_2O$); 4.37 (d, J = 5 Hz, 1H : H at 2); 4.54 (AB, J = 9 Hz, 2H : CH_2 at 20); 4.76 (broad d, J = 10 Hz, 1H : H at 5); 4.81 (dd, J = 9 and 3 Hz, 1H : H at 13); 6.51 (s, 1H : H at 10).

1β,2α-Carbonato-4α,10β-dihydroxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-11-taxene may

be prepared in the following way:

To a solution of 0.400 g of 7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-1β,2α,4α,10β-tetrahydroxy-11-taxene in 10 cm^3 of dichloromethane are added, with stirring and at a temperature in the region of -78°C, 1 cm^3 of pyridine and 0.560 g of triphosgene. The reaction mixture is stirred for 2 hours at a temperature in the region of -78°C and the reaction medium is then allowed to warm slowly to a temperature in the region of 20°C. 30 cm^3 of saturated aqueous ammonium chloride solution and 20 cm^3 of dichloromethane are added. The organic phase is separated out after settling of the phases has taken place, washed with twice 40 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 0.400 g of a yellow foam is obtained, which is purified by chromatography on 25 g of silica (0.063-0.2 mm) contained in a column 2 cm in diameter (eluent: ethyl acetate/cyclohexane : 20/80 by volume), collecting 10 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 0.330 g of 1β,2α-carbonato-4α,10β-dihydroxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-11-taxene is obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 0.54 (mt,

6H : CH_2 ethyl); 0.63 (mt, 6H : CH_2 ethyl); 0.92 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.03 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.11 (s, 3H : CH_3); 1.19 (s, 3H : CH_3); 1.72 (s, 3H : CH_3); 1.98 and 2.46 (2 mts, 1H each : CH_2 at 6); 2.06 (s, 3H : CH_3); 2.55 at 2.66 (2 dd, J = 16 and 9 Hz and J = 16 and 3 Hz respectively, 1H each: CH_2 at 14); 3.00 (s, 1H : OH at 4); 3.13 (d, J = 5 Hz, 1H : H at 3); 4.06 (dd, J = 11 and 7 Hz, 1H : H at 7); 4.20 (d, J = 2.5 Hz, 1H : OH at 10); 4.33 (d, J = 5 Hz, 1H : H at 2); 4.55 (AB, J = 9 Hz, 2H : CH_2 at 20); 4.76 (broad d, J = 10 Hz, 1H : H at 5); 4.82 (dd, J = 9 and 3 Hz, 1H : H at 13); 5.19 (d, J = 2.5 Hz, 1H : H at 10).

7β,13α-Bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-1β,2α,4α,10β-tetrahydroxy-11-taxene may be prepared in the following way:

To a solution of 3.80 g of 5β,20-epoxy-9-oxo-1β,2α,4α,10β,13α-pentahydroxy-7β-triethylsilyloxy-11-taxene in 100 cm^3 of dichloromethane are added, with stirring and at a temperature in the region of 0°C, 1.20 cm^3 of pyridine and 2.48 cm^3 of chlorotriethylsilane. The reaction mixture is stirred for 3 hours at a temperature in the region of 0°C. 100 cm^3 of saturated aqueous sodium chloride solution are added. The organic phase is separated out after settling of the phases has taken place, washed with twice 100 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate,

filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 5.34 g of an orange-coloured oil are obtained, which product is purified by chromatography on 300 g of silica (0.063-0.2 mm) contained in a column 3 cm in diameter (eluent: ethyl acetate/cyclohexane : 25/75 by volume), collecting 40 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 4.18 g of of 7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-1β,2α,4α,10β-tetrahydroxy-11-taxene are obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 0.53 (mt, 6H : CH_2 ethyl); 0.75 (mt, 6H : CH_2 ethyl); 0.91 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.01 (s, 3H : CH_3); 1.03 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.09 (s, 3H : CH_3); 1.63 (s, 3H : CH_3); 1.97 (s, 3H : CH_3); from 1.95 to 2.10 and 2.40 (2 mts, 2H each : CH_2 at 14 and CH_2 at 6); 3.17 (s, 1H : OH); 3.18 (d, J = 5.5 Hz, 1H : H at 3); 3.43 (d, J = 10 Hz, 1H : OH at 2); 3.76 (dd, J = 10 and 5.5 Hz, 1H : H at 2); 3.96 (dd, J = 11 and 6 Hz, 1H : H at 7); 4.10 (s, 1H : OH); 4.18 (d, J = 3 Hz, 1H : OH at 10); 4.44 and 4.73 (2d, J = 9 Hz, 1H each: CH_2 at 20); 4.64 (broad d, J = 10 Hz, 1H : H at 5); 4.74 (mt, 1H : H at 13); 5.14 (d, J = 3 Hz, 1H : H at 10).

EXAMPLE 2

To a solution of 20.5 mg of 5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate in 0.2 cm^3 of acetonitrile and 0.025 cm^3 of tetrahydrofuran are added 45 mg of sodium chloride and a spatulaful of activated 4Å molecular sieves. The mixture obtained is maintained at reflux, for 2 hours, under an argon atmosphere. After cooling to a temperature in the region of 20°C, the solvents are evaporated off under reduced pressure (0.27 kPa) at a temperature in the region of 40°C, and the solid residue is taken up in 5 cm^3 of dichloromethane, filtered on cotton wool and rinsed with 5 cm^3 of an ethyl acetate/dichloromethane mixture (50/50 by volume). The organic phases are concentrated under reduced pressure (0.27 kPa) at a temperature in the region of 40°C. 17.1 mg of a yellow foam are thus obtained, which product is purified by thin-layer preparative chromatography [2 Merck preparative plates, Kieselgel 60F254, thickness 0.25 mm, deposited as a solution in dichloromethane, eluent: methanol/dichloromethane mixture (6/94 by volume)]. After elution of the zone corresponding to the main product with a methanol/dichloromethane mixture (10/90 by volume), filtration on sintered glass and then evaporation of the solvents under reduced pressure

(0.27 kPa) at a temperature in the region of 40°C, 10.0 mg of 5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-7,8β-methylene-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-19-nor-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate are obtained in the form of a white resin, the characteristics of which are as follows:

- ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 1.18 (t, J = 7.5 Hz, 3H : CH_3 ethyl); 1.22 (s, 6H : CH_3); 1.32 (s, 9H : $C(CH_3)_3$); 1.41 (mt, 1H : H at 7); 1.69 and 2.23 (2 mts, 1H each : CH_2 at 19); 1.81 (s, 1H : OH at 1); 1.85 (s, 3H : CH_3); 2.12 and 2.50 (d and dt respectively, J = 16 and J = 16 and 4.5 Hz, 1H each : CH_2 at 6); 2.25 and 2.39 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 2.63 (mt, 2H : CH_2 ethyl); 3.23 (mt, 1H : OH at 2'); 3.52 (s, 3H : OCH_3); 4.03 (d, J = 7 Hz, 1H : H at 3); 4.12 and 4.44 (2d, J = 9 Hz, 1H each : CH_2 at 20); 4.20 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.62 (mt, 1H : H at 2'); 4.70 (d, J = 4 Hz, 1H : H at 5); 5.22 (mt, 1H : H at 3'); 5.28 (d, J = 10 Hz, 1H : CONH); 5.58 (d, J = 7 Hz, 1H : H at 2); 6.23 (broad t, J = 9 Hz, 1H : H at 13); 6.41 (s, 1H : H at 10); 7.18 (dd, J = 5 and 3.5 Hz, 1H : H at 4 of the 2-thenoyl); from 7.30 to 7.50 (mt, 5H : aromatic H at 3'); 7.67 (broad d, J = 5 Hz, 1H : H at 5 of the 2-thenoyl); 7.96 (broad d, J = 3.5 Hz, 1H : H at 5 of the 2-thenoyl).

5β,20-Epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β-

trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate may be prepared in the following way:

A solution of 75 mg of 5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate in 0.77 cm^3 of a 0.1N solution of hydrochloric acid in ethanol is stirred at a temperature in the region of 5°C for 2 hours. The reaction mixture is then diluted with 10 cm^3 of dichloromethane and washed with twice 1 cm^3 of distilled water. After extraction of the aqueous phase with 1 cm^3 of dichloromethane, the organic phases are combined, dried over magnesium sulphate, filtered on sintered glass and concentrated under reduced pressure (0.27 kPa) at a temperature in the region of 40°C. 74.4 mg of a yellow resin are thus obtained, which product is purified by chromatography at atmospheric pressure on 8 g of silica (0.063-0.2 mm) contained in a column 1.5 cm in diameter (elution gradient: ethyl acetate/dichloromethane from 5/95 to 20/80 by volume), collecting 8 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (0.27 kPa) at 40°C for 2 hours. 56.3 mg of 5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β-

trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate are thus obtained in the form of a pale yellow foam, the characteristics of which are as follows:

- ^{1}H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : 1.20 (s, 6H : CH_3); 1.22 (t, J = 7.5 Hz, 3H : CH_3 ethyl); 1.36 (s, 9H : $C(CH_3)_3$); 1.71 (s, 1H : OH at 1); 1.89 (s, 3H : CH_3); 2.05 (s, 3H : CH_3); 2.25 and 2.86 (2 mts, 1H each : CH_2 at 6); 2.33 (d, J = 9 Hz, 2H : CH_2 at 14); 2.66 (mt, 2H : CH_2 ethyl); 3.28 (d, J = 5 Hz, 1H : OH at 2'); 3.52 (s, 3H : OCH_3); 3.90 (d, J = 7 Hz, 1H : H at 3); 4.20 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.27 and 4.50 (2d, J = 9 Hz, 1H each : CH_2 at 20); 4.61 (mt, 1H : H at 2'); 4.88 (broad d, J = 10 Hz, 1H : H at 5); 5.20 (broad d, J = 10 Hz, 1H : H at 3'); 5.30 (d, J = 10 Hz, 1H : CONH); 5.50 (dd, J = 10 and 7 Hz, 1H : H at 7); 5.65 (d, J = 7 Hz, 1H : H at 2); 6.18 (broad t, J = 9 Hz, 1H : H at 13); 6.70 (s, 1H : H at 10); 7.18 (dd, J = 5 and 3.5 Hz, 1H : H at 4 of the 2-thenoyl); from 7.30 to 7.50 (mt, 5H : aromatic H at 3'); 7.69 (dd, J = 5 and 1.5 Hz, 1H : H at 5 of the 2-thenoyl); 7.92 (dd, J = 3.5 and 1.5 Hz, 1H : H at 5 of the 2-thenoyl).

5β,20-Epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate may be prepared in the following way:

To a solution of 55.2 mg of 5β,20-epoxy-1β,13α-dihydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β-trifluoromethanesulphonyloxy-11-taxene in 0.1 cm^3 of anhydrous toluene are successively added 41 mg of (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylic acid, 26 mg of dicyclohexylcarbodiimide and 3 mg of 4-(N,N-dimethylamino)pyridine. The reaction mixture is stirred for 2 hours, under an argon atmosphere and at a temperature in the region of 20°C, and then placed on a chromatography column at atmospheric pressure (15 g of silica (0.063-0.2 mm) contained in a column 1.5 cm in diameter (elution gradient: ethyl acetate/dichloromethane from 5/95 to 10/90 by volume), collecting 10 cm^3 fractions). The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (0.27 kPa) at 40°C for 2 hours. 75.3 mg of 5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate are thus obtained in the form of a white foam, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.04 (s, 9H : $C(CH_3)_3$); 1.04 (t, J = 7.5 Hz, 3H : CH_3 ethyl); 1.14 (s, 3H : CH_3); 1.16 (s, 3H : CH_3); 1.61 (s, 1H : OH

at 1); 1.68 (s, 3H : CH_3); 1.81 (s, 3H : CH_3); from 2.00 to 2.30 (mt, 4H : CH_2 ethyl and CH_2 at 14); 2.03 and 2.80 (2 mts, 1H each : CH_2 at 6); 3.50 (s, 3H : OCH_3); 3.77 (d, J = 7 Hz, 1H : H at 3); 3.81 (s, 3H : $ArOCH_3$); 4.13 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.18 and 4.39 (2d, J = 9 Hz, 1H each : CH_2 at 20); 4.48 (d, J = 4 Hz, 1H : H at 2'); 4.78 (broad d, J = 10 Hz, 1H : H at 5); from 5.35 to 5.50 (mt, 2H : H at 3' and H at 7); 5.55 (d, J = 7 Hz, 1H : H at 2); 5.96 (broad t, J = 9 Hz, 1H : H at 13); 6.34 (mt, 1H : H at 5'); 6.56 (s, 1H : H at 10); 6.88 (d, J = 8 Hz, 2H : aromatic H ortho to the OCH_3); 7.13 (dd, J = 5 and 3.5 Hz, 1H : H at 4 of the 2-thenoyl); from 7.30 to 7.45 (mt, 5H : aromatic H at 3'); 7.36 (d, J = 8 Hz, 2H : aromatic H meta to the OCH_3); 7.62 (broad d, J = 5 Hz, 1H : H at 5 of the 2-thenoyl); 7.80 (broad d, J = 3.5 Hz, 1H : H at 5 of the 2-thenoyl).

5β,20-Epoxy-1β,13α-dihydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β-trifluoromethanesulphonyloxy-11-taxene may be prepared in the following way:

To a solution of 50 mg of 5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-1β,7β,13α-trihydroxy-11-taxene in 0.5 cm^3 of anhydrous dichloromethane and 0.0255 cm^3 of pyridine, maintained under an argon atmosphere and at a temperature in the region of 0°C, is added dropwise 0.0265 cm^3 of trifluoromethanesulphonic anhydride. The orange-

coloured solution obtained is stirred for 10 minutes at a temperature in the region of 0°C and for 45 minutes at a temperature in the region of 20°C, followed by addition of 0.1 cm^3 of a methanol/dichloromethane mixture (5/95 by volume). The solution is placed on a chromatography column at atmospheric pressure (10 g of silica (0.063-0.2 mm) contained in a column 1.5 cm in diameter (elution gradient: methanol/dichloromethane from 2/98 to 5/95 by volume), collecting 8 cm^3 fractions). The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (0.27 kPa) at 40°C for 2 hours. 55.2 mg of 5β,20-epoxy-1β,13α-dihydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β-trifluoromethanesulphonyloxy-11-taxene are thus obtained in the form of a white foam.

5β,20-Epoxy-1β,7β,13α-trihydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-11-taxene may be prepared in the following way:

To a solution of 0.302 g of 5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β,13α-bis(triethylsilyloxy)-11-taxene in 5 cm^3 of dichloromethane are added, at a temperature in the region of 20°C, 6 cm^3 of triethylamine-hydrofluoric acid complex ($Et_3N.3HF$). The reaction mixture is stirred for 24 hours at a temperature in the region of 20°C, followed by addition of 50 cm^3 of dichloromethane and 100 cm^3 of saturated aqueous sodium hydrogen carbonate.

solution. The organic phase is separated out after settling of the phases has taken place, washed with twice 40 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 0.24 g of 5β,20-epoxy-1β,7β,13α-trihydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-11-taxene is thus obtained in the form of a white foam, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm): 1.07 (s, 3H : CH_3); 1.10 (s, 3H : CH_3); 1.22 (t, J = 7.5 Hz, 3H : CH_3 ethyl); 1.62 (s, 1H : OH at 1); 1.69 (s, 3H : CH_3); 1.89 and 2.63 (2 mts, 1H each: CH_2 at 6); 2.03 (d, J = 5.5 Hz, 1H : OH at 13); 2.07 (s, 3H : CH_3); 2.27 (d, J = 9 Hz, 2H : CH_2 at 14); 2.35 (d, J = 4.5 Hz, 1H : OH at 7); 2.59 (mt, 2H : CH_2 ethyl); 3.52 (s, 3H : OCH_3); 3.84 (d, J = 7 Hz, 1H : H at 3); 4.23 and 4.43 (2d, J = 9 Hz, 1H each : CH_2 at 20); 4.25 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.49 (mt, 1H : H at 7); 4.87 (mt, 1H : H at 13); 4.95 (broad d, J = 10Hz, 1H : H at 5); 5.53 (d, J = 7 Hz, 1H : H at 2); 6.42 (s, 1H : H at 10); 7.14 (dd, J = 4.5 and 3.5 Hz, 1H : H at 4 of the 2-thenoyl); 7.61 (dd, J = 4.5 and 1.5 Hz, 1H : H at 5 of the 2-thenoyl); 7.83 (dd, J = 3.5 and 1.5 Hz, 1H : H at 3 of the 2-thenoyl).

5β,20-Epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β,13α-

bis(triethylsilyloxy)-11-taxene may be prepared in the following way:

To a solution of 0.5 g of 5β,20-epoxy-1β,10β-dihydroxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β,13α-bis(triethylsilyloxy)-11-taxene in 10 cm^3 of pyridine is added, at a temperature in the region of 0°C, 0.286 cm^3 of methoxyacetyl chloride. The reaction mixture is stirred for 10 hours at a temperature in the region of 20°C, followed by addition of 100 cm^3 of dichloromethane and 50 cm^3 of saturated aqueous ammonium chloride solution. The organic phase is separated out after settling of the phases has taken place, washed with twice 40 cm^3 of saturated aqueous ammonium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. The residue obtained (0.6 g) is purified by chromatography on 50 g of silica (0.063-0.2 mm) contained in a column 2 cm in diameter (eluent: ethyl acetate/cyclohexane : 5/95 by volume), collecting 10 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (0.27 kPa) at 40°C. 0.320 g of 5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β,13α-bis(triethylsilyloxy)-11-taxene is obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz, $CDCl_3$, δ in ppm) : from 0.50

to 0.70 (mt, 12 H : CH_2 ethyl) : 0.92 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 0.98 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.09 (s, 3H : CH_3); 1.15 (s, 3H : CH_3); 1.27 (t, J = 7.5 Hz, 3H : CH_3 ethyl at 4); 1.59 (s, 1H : OH at 1); 1.65 (s, 3H : CH_3); 1.85 and 2.52 (2 mts, 1H each : CH_2 at 6); 2.07 and 2.18 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 2.08 (s, 3H : CH_3); 2.58 (mt, 2H : CH_2 ethyl at 4); 3.50 (s, 3H : OCH_3); 3.73 (d, J = 7 Hz, 1H : H at 3); 4.13 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.20 and 4.41 (2d, J = 9 Hz, 1H each : CH_2 at 20); 4.49 (dd, J = 11 and 7 Hz, 1H : H at 7); 4.89 (broad t, J = 9 Hz, 1H = H at 13); 4.91 (broad d, J = 10 Hz, 1H : H at 5); 5.53 (d, J = 7 Hz, 1H : H at 2); 6.51 (s, 1H : H at 10); 7.12 (dd, J = 4.5 and 3 Hz, 1H : H at 4 of the 2-thenoyl); 7.61 (d, J = 4.5 Hz, 1H : H at 5 of the 2-thenoyl); 7.83 (d, J = 3 Hz, 1H : H at 3 2-thenoyl).

5β,20-Epoxy-1β,10β-dihydroxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β,13α-bis(triethylsilyloxy)-11-taxene may be prepared in the following way:

To a solution of 0.5 g of 1β,2α-carbonyldioxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-propanoyloxy-7β,13α-bis(triethylsilyloxy)-11-taxene in 20 cm^3 of tetrahydrofuran, under an argon atmosphere and at a temperature in the region of -78°C, are added 1.5 cm^3 of a 1M solution of 2-thienyllithium in tetrahydrofuran. The reaction mixture is stirred for 35 minutes at a temperature in the region of -78°C,

followed by addition of 1 cm^3 of saturated aqueous ammonium chloride solution. At a temperature in the region of 20°C, 10 cm^3 of saturated aqueous ammonium chloride solution and 50 cm^3 of dichloromethane are added. The organic phase is separated out after settling of the phases has taken place, washed with twice 10 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 0.65 g of a solid is obtained, which is purified by chromatography on 90 g of silica (0.063-0.2 mm) contained in a column 1 cm in diameter (eluent: ethyl acetate/cyclohexane : 10/90 by volume), collecting 10 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (0.27 kPa) at 40°C. 0.511 g of 5β,20-epoxy-1β,10β-dihydroxy-9-oxo-4α-propanoyloxy-2α-(2-thenoyloxy)-7β,13α-bis(triethylsilyloxy)-11-taxene is obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR (600 MHz, $CDCl_3$, δ in ppm): 0.57 (mt, 6 H : CH_2 ethyl); 0.68 (mt, 6 H : CH_2 ethyl); 0.95 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.01 (t, J = 7.5 Hz, 9H : CH_3 ethyl); 1.07 (s, 3H : CH_3); 1.17 (s, 3H : CH_3); 1.27 (t, J = 7.5 Hz, 3H : CH_3 ethyl at 4); 1.73 (s, 3H : CH_3); 1.90 and 2.47 (2 mts, 1H each; CH_2 at 6); 2.02 (s, 3H : CH_3); 2.09 and 2.18 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at

14); 2.60 (mt, 2H : CH_2 ethyl at 4); 3.82 (d, J = 7 Hz, 1H : H at 3); 4.24 and 4.44 (2d, J = 9 Hz, 1H each : CH_2 at 20); 4.26 (d, J = 0.5 Hz, 1H : OH at 10); 4.42 (dd, J = 11 and 7 Hz, 1H : H at 7); 4.93 (broad d, J = 10 Hz, 1H : H at 5); 4.97 (broad t, J = 9 Hz, 1H : H at 13); 5.13 (d, J = 0.5 Hz, 1H : H at 10); 5.53 (d, J = 7 Hz, 1H : H at 2); 7.15 (dd, J = 4.5 and 3 Hz, 1H : H at 4 of the 2-thenoyl); 7.63 (d, J = 4.5 Hz, 1H : H at 5 of the 2-thenoyl); 7.85 (d, J = 3 Hz, 1H : H at 3 of the 2-thenoyl).

EXAMPLE 3

To a solution of 154 mg of 2α-benzoyloxy-4α-butanoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate in 2 cm^3 of acetonitrile and 200 μl of tetrahydrofuran are successively added 96 mg of powdered 4Å molecular sieves and 225 mg of sodium chloride. The reaction mixture is kept stirring at a temperature in the region of 75°C for 5 hours, followed, at a temperature in the region of 20°C, by addition of 15 cm^3 of dichloromethane and 10 cm^3 of saturated aqueous sodium chloride solution. The organic phase is separated out after settling of the phases has taken place, washed with twice 20 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to

dryness under reduced pressure (2.7 kPa) at 40°C. 133 mg of product are obtained, which product is purified by chromatography on 80 g of silica (0.063-0.2 mm) contained in a column 1 cm in diameter, eluting with a dichloromethane/methanol mixture (98/2 by volume) and collecting 10 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 63 mg of 2α-benzoyloxy-4α-butanoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-7β,8-methylene-19-nor-9-oxo-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate are obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^{1}H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 of the propyl); 1.26 (s, 6H : CH_3); 1.31 (s, 9H : $C(CH_3)_3$); 1.42 (mt, 1H : H at 7); 1.71 and 2.26 (2 mts, 1H each : CH_2 at 19); from 1.60 to 1.85 (mt, 2H : CH_2 of the propyl); 1.86 (s, 3H : CH_3); 1.88 (s, 1H : OH at 1); 2.12 and 2.50 (broad d and mt respectively, J = 16 Hz, 1H each : CH_2 at 6); 2.23 and 2.39 (mt and dd respectively, J = 16 and 9 Hz, 2H : CH_2 at 14); 2.49 and 2.65 (2 mts, 1H each : $OCOCH_2$ of the propyl); 3.25 (mt, 1H : OH at 2'); 3.51 (s, 3H : OCH_3); 4.05 and 4.32 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.10 (d, J = 7 Hz, 1H : H at 3); 4.16 and 4.22 (2 d, J = 16 Hz, 1H each: $OCOCH_2O$); 4.62 (mt, 1H : H at 2'); 4.68 (broad d, J = 4.5 Hz, 1H : H at 5); 5.25 (broad d, J =

10 Hz, 1H : H at 3'); 5.30 (d, J = 10 Hz, 1H : CONH); 5.65 (d, J = 7 Hz, 1H : H at 2); 6.23 (broad t, J = 9 Hz, 1H : H at 13); 6.42 (s, 1H : H at 10); from 7.25 to 7.45 (mt, 5H : aromatic H at 3'); 7.51 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.62 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.16 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

2α-Benzoyloxy-4α-butanoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate may be prepared in the following way:

A solution of 400 mg of 2α-benzoyloxy-4α-butanoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate in 6.4 cm^3 of 0.1N hydrochloric ethanol solution is kept stirring at a temperature in the region of 0°C for 6 hours, and then at a temperature in the region of 20°C for 15 hours. The reaction medium is concentrated to dryness under reduced pressure (2.7 kPa) at 20°C. The crude reaction product is dissolved in 20 cm^3 of dichloromethane and 10 cm^3 of saturated aqueous sodium bicarbonate solution. The aqueous phase is separated out after settling of the phases has taken place and then extracted with twice 20 cm^3 of dichloromethane. The organic phases are combined, washed with 30 cm^3 of distilled water and then

dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 20°C. 410 mg of a product are obtained, which product is purified by chromatography on 60 g of silica (0.063-0.2 mm) contained in a column 1 cm in diameter, eluting with a dichloromethane/methanol mixture (98.5/1.5 by volume) and collecting 10 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 20°C. 307 mg of 2α-benzoyloxy-4α-butanoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate are obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm): 0.93 (t, J = 7.5 Hz, 3H : CH_3 of the propyl); 1.22 (s, 3H : CH_3); 1.24 (s, 3H : CH_3); 1.35 (s, 9H : $C(CH_3)_3$); from 1.65 to 1.85 (mt, 2H : CH_2 of the propyl); 1.74 (s, 1H : OH at 1); 1.88 (s, 3H : CH_3); 2.04 (s, 3H : CH_3); 2.25 and 2.86 (2 mts, 1H each : CH_2 at 6); 2.33 (d, J = 9 Hz, 2H : CH_2 at 14); 2.52 and 2.66 (2 mts, J = 14.5 and 6.5 Hz, 1H each : $OCOCH_2$ of the propyl); 3.33 (d, J = 4 Hz, 1H : OH at 2'); 3.52 (s, 3H : OCH_3); 3.94 (d, J = 7 Hz, 1H : H at 3); 4.16 and 4.21 (2 d, J = 16 Hz, 1H each: $OCOCH_2O$); 4.19 and 4.35 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.62 (mt, 1H : H at 2'); 4.86 (broad d, J =

10 Hz, 1H : H at 5); 5.22 (broad d, J = 10 Hz, 1H : H at 3'); 5.33 (d, J = 10 Hz, 1H : CONH); 5.50 (dd, J = 11 and 8 Hz, 1H : H at 7); 5.73 (d, J = 7 Hz, 1H : H at 2); 6.16 (broad t, J = 9 Hz, 1H : H at 13); 6.71 (s, 1H : H at 10); from 7.25 to 7.45 (mt, 5H : aromatic H at 3'); 7.51 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.63 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.12 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ at ortho-H).

2α-Benzoyloxy-4α-butanoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate may be prepared in the following way:

To a solution of 400 mg of 2α-benzoyloxy-4α-butanoyloxy-1β,13α-dihydroxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxene in 10 cm^3 of anhydrous ethyl acetate are successively added 247 mg of (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylic acid, 186 mg of dicyclohexylcarbodiimide and 12.5 mg of 4-dimethylaminopyridine. The reaction mixture is stirred for 15 hours, under an argon atmosphere and at a temperature in the region of 20°C, and then concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 1 g of a product is obtained, which is purified by chromatography on 100 g of silica

(0.063-0.2 mm) contained in a column 3 cm in diameter, eluting with a dichloromethane/methanol mixture (95/5 by volume) and collecting 12 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 410 mg of 2α-benzoyloxy-4α-butanoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate are obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm): 0.92 (t, J = 7.5 Hz, 3H : CH_3 of the propyl); 1.07 (s, 9H : $C(CH_3)_3$); 1.17 (s, 6H : CH_3); from 1.55 to 1.70 (mt, 3H : CH_2 of the propyl and OH at 1); 1.64 (s, 3H : CH_3); 1.84 (s, 3H : CH_3); 2.08 and from 2.15 to 2.30 (dd and mt respectively, J = 16 and 9 Hz, 1H each : CH_2 at 14); from 2.15 to 2.30 and 2.82 (2 mts, 1H each : CH_2 at 6); from 2.15 to 2.30 (mt, 2H : $OCOCH_2$ of the propyl); 3.51 (s, 3H : OCH_3); 3.82 (s, 3H : $ArOCH_3$); 3.83 (d, J = 7 Hz, 1H : H at 3); 4.12 and 4.28 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.14 and 4.22 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.52 (broad d, J = 4.5 Hz, 1H : H at 2'); 4.79 (broad d, J = 10 Hz, 1H : H at 5); from 5.35 to 5.50 (mt, 1H : H at 3'); 5.44 (dd, J = 9 and 7 Hz, 1H : H at 7); 5.67 (d, J = 7 Hz, 1H : H at 2); 5.99 (broad t, J = 9 Hz, 1H : H at 13); 6.40 (mult., 1H : H

at 5'); 6.59 (s, 1H : H at 10); 6.92 (d, J = 8.5 Hz, 2H aromatic H ortho to the OCH_3); from 7.25 to 7.45 (mt, 5H : aromatic H at 3'); 7.37 (d, J = 8.5 Hz, 2H : aromatic meta to the OCH_3); 7.48 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.63 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.11 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

The 2α-Benzoyloxy-4α-butanoyloxy-1β,13α-dihydroxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxene may be prepared in the following way:

To a solution of 389 mg of 2α-benzoyloxy-4α-butanoyloxy-5β,20-epoxy-10β-methoxyacetoxyl-9-oxo-1β,7β,13α-trihydroxy-11-taxene in 6 cm^3 of anhydrous dichloromethane and 390 μl of pyridine, maintained under an argon atmosphere and at a temperature in the region of 0°C, are added dropwise 410 μl of trifluoromethanesulphonic anhydride. The orange-coloured solution obtained is stirred for 15 minutes at a temperature in the region of 0°C, followed by addition of 3 cm^3 of water and 50 cm^3 of dichloromethane. The organic phase is separated out after settling of the phases has taken place, washed with twice 40 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 510 mg of product are obtained, which product is purified by chromatography on 70 g of silica (0.063-0.2 mm) contained in a column

1 cm in diameter, eluting with a dichloromethane/methanol mixture (95/5 by volume) and collecting 10 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 410 mg of 2α-benzoyloxy-4α-butanoyloxy-1β,13α-dihydroxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxene are obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$, δ in ppm): 1.06 (t, J = 7.5 Hz, 3H : CH_3 of the propyl); 1.06 (s, 3H : CH_3); 1.20 (s, 3H : CH_3); 1.63 (s, 1H : OH at 1); 1.77 (mt, 2H : CH_2 of the propyl); 1.87 (s, 3H : CH_3); 2.18 (d, J = 5 Hz, 1H : OH at 13); from 2.15 to 2.40 (limiting AB, 2H : CH_2 14); from 2.15 to 2.40 and 2.89 (2 mts, 1H each : CH_2 6); 2.25(s, 3H : CH_3); 2.59 (limiting AB, J = 16 and 7.5 Hz, 2H : $OCOCH_2$ of the propyl); 3.51 (s, 3H : OCH_3); 4.03 (d, J = 7 Hz, 1H : H3); 4.16 and 4.24 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.18 and 4.35 (2 d, J = 9 Hz, 1H each : CH_2 20); 4.85 (mt, 1H : H13); 4.92 (broad d, J = 10 Hz, 1H : H5); 5.57 (dd, J = 10.5 and 7 Ez, 1H : H 7); 5.68 (d, J = 7 Hz, 1H : H 2); 6.73 (s, 1H : H 10); 7.51 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.63 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.10 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

2α-Benzoyloxy-4α-butanoyloxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-1β,7β,13α-trihydroxy-11-taxene may

be prepared in the following way:

To a solu*ion of 580 mg of 2α-benzoyloxy-4α-butanoyloxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-11-taxene in 5 cm^3 of dichloromethane are added, at a temperature in the region of 20°C, 5.5 cm^3 of triethylamine-hydrofluoric acid complex. The reaction mixture is stirred for 23 hours at a temperature in the region of 20°C, followed by addition of 50 cm^3 of dichloromethane and 100 cm^3 of saturated aqueous sodium hydrogen carbonate solution. The organic phase is separated out after settling of the phases has taken place, washed with twice 20 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 520 mg of product are obtained, which product is purified by chromatography on 70 g of silica (0.063-0.2 mm) contained in a column 2 cm in diameter, eluting with a methanol/dichloromethane mixture (5/95 by volume) and collecting 10 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 389 mg of 2α-benzoyloxy-4α-butanoyloxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-1β,7β,13α-trihydroxy-11-taxene are obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 1.05 (t,

$J = 7.5$ Hz, 3H : CH_3 of the propyl); 1.11 (s, 6H : CH_3); 1.67 (s, 3H : CH_3); 1.71 (s, 1H : OH at 1); 1.75 (mt, 2H : CH_2 of the propyl); 1.85 and from 2.45 to 2.65 (2 mts, 1H each : CH_2 at 6); 2.05 (s, 3H : CH_3); 2.24 (d, $J = 5$ Hz, 1H : OH); 2.28 (limiting AB; $J = 16$ and 9 Hz, 2H : CH_2 at 14); 2.40 (d, $J = 4$ Hz, 1H : OH); 2.56 (limiting AB, 2H : $OCOCH_2$ of the propyl); 3.51 (s, 3H : OCH_3); 3.88 (d, $J = 7$ Hz, 1H : H at 3); 4.15 and 4.32 (2 d, $J = 9$ Hz, 1H each : CH_2 at 20); 4.23 (limiting AB, $J = 16$ Hz, 2H : $OCOCH_2O$); 4.48 (mt, 1H : H at 7); 4.86 (mt, 1H : H at 13); 4.94 (broad d, $J = 10$ Hz, 1H : H at 5); 5.62 (d, $J = 7$ Hz, 1H : H at 2); 6.43 (s, 1H : H at 10); 7.49 (t, $J = 7.5$ Hz, 2H : $OCOC_6H_5$ meta-H); 7.62 (t, $J = 7.5$ Hz, 1H : $OCOC_6H_5$ para-H); 8.12 (d, $J = 7.5$ Hz, 2H : $OCOC_6H_5$ ortho-H).

2α-Benzoyloxy-4α-butanoyloxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-11-taxene may be prepared in the following way:

To a solution of 906 mg of 2α-benzoyloxy-4α-butanoyloxyl-1β,10β-dihydroxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-11-taxene in 18 cm^3 of pyridine are added, at a temperature in the region of 0°C, 1.03 cm^3 of methoxyacetyl chloride. The reaction mixture is stirred for 14 hours at a temperature in the region of 20°C, followed by addition of 20 cm^3 of dichloromethane and 20 cm^3 of saturated aqueous ammonium chloride solution. The organic phase

is separated out after settling of the phases has taken place, washed with 4 times 20 cm^3 of saturated aqueous copper sulphate solution, with twice 40 cm^3 of saturated aqueous ammonium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 800 mg of a product are obtained, which product is purified by chromatography on 100 g of silica (0.063-0.2 mm) contained in a column 2.5 cm in diameter, eluting with a methanol/dichloromethane mixture (2/98 by volume) and collecting 15 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 580 mg of 2α- benzoyloxy-4α-butanoyloxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-11-taxene are obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 0.60 and 0.68 (2 mts, 6H each : CH_2 of the ethyl); 0.95 and 1.04 (2 t, J = 7.5 Hz, 9H each : CH_3 of the ethyl); 1.09 (t, J = 7.5 Hz, 3H : CH_3 of the propyl); 1.13 (s, 3H : CH_3); 1.18 (s, 3H : CH_3); 1.64 (s, 1H : OH at 1); 1.68 (s, 3H : CH_3); 1.84 (mt, 2H : CH_2 of the propyl); 1.89 and 2.50 (2 mts, 1H each : CH_2 at 6); 2.11 and 2.23 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 2.13 (s, 3H : CH_3); 2.55 (mt, 2H : $OCOCH_2$ of the propyl); 3.53 (s, 3H : OCH_3); 3.82 (d, J = 7 Hz, 1H : H at 3); 4.13

and 4.31 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.16 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.52 (dd, J = 11 and 7 Hz, 1H : H at 7); 4.91 (mt, 1H : H at 13); 4.93 (broad d, J = 10 Hz, 1H : H at 5); 5.64 (d, J = 7 Hz, 1H : H at 2); 6.54 (s, 1H : H at 10); 7.47 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ at meta-H); 7.61 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.11 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

2α-Benzoyloxy-4α-butanoyloxy-1β,10β-dihydroxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-11-taxene may be prepared in the following way:

To a solution of 907 mg of 4α-butanoyloxy-1β,2α-carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-11-taxene in 50 cm^3 of anhydrous tetrahydrofuran are added, at a temperature in the region of -78°C, 2.34 cm^3 of a 1M solution of phenyllithium in tetrahydrofuran. The reaction mixture is stirred for 1 hour at a temperature in the region of -78°C, followed by addition of 10 cm^3 of saturated aqueous ammonium chloride solution. At a temperature in the region of 20°C, 20 cm^3 of saturated aqueous ammonium chloride solution and 50 cm^3 of dichloromethane are added. The organic phase is separated out after settling of the phases has taken place, washed with twice 10 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 1.3 g of product are

obtained, which product is purified by chromatography on 150 g of silica (0.063-0.2 mm) contained in a column 5 cm in diameter, eluting with an ethyl acetate/cyclohexane mixture (10/90 by volume) and collecting 18 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 906 mg of 2α-benzoyloxy-4α-butanoyloxyl-1β,10β-dihydroxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-11-taxene are obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 0.56 and 0.67 (2 mts, 6H each : CH_2 of the ethyl); 0.95 and 1.03 (2 t, J = 7.5 Hz, 9H each : CH_3 of the ethyl); 1.08 (s, 3H : CH_3); 1.10 (t, J = 7.5 Hz, 3H : CH_3 of the propyl); 1.18 (s, 3H : CH_3); 1.60 (s, 1H : OH at 1); 1.73 (s, 3H : CH_3); 1.84 (mt, 2H : CH_2 of the propyl); 1.91 and 2.48 (2 mts, 1H each : CH_2 at 6); 2.03 (s, 3H : CH_3); 2.11 and 2.22 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 2.58 (mt, 2H : $OCOCH_2$ of the propyl); 3.87 (d, J = 7 Hz, 1H : H at 3); 4.18 and 4.32 (2d, J = 9 Hz, 1H each : CH_2 at 20); 4.28 (d, J = 2 Hz, 1H : OH at 10); 4.42 (dd, J = 10.5 and 6.5 Hz, 1H : H at 7); 4.93 (broad d, J = 10 Hz, 1H : H at 5); 4.98 (t, J = 9 Hz, 1H : H at 13); 5.17 (d, J = 2 Hz, 1H : H at 10); 5.62 (d, J = 7 Hz, 1H : H at 2); 7.49 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ at meta-H); 7.61 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.12 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

4α-Butanoyloxy-1β,2α-carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-11-taxene may be prepared in the following way:

To a solution of 870 mg of 1β,2α-carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-4α-hydroxy-10β-methoxyacetoxy-9-oxo-11-taxene in 15 cm^3 of dichloromethane are added 1.46 g of 4-dimethylaminopyridine and 3.90 cm^3 of butyric anhydride. The reaction medium is heated at a temperature in the region of 42°C for 45 hours. 50 cm^3 of saturated aqueous sodium chloride solution and 50 cm^3 of dichloromethane are added. The organic phase is separated out after settling of the phases has taken place, washed with twice 40 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 2.0 g of product are obtained, which product is purified by chromatography on 170 g of silica (0.063-0.2 mm) contained in a column 3 cm in diameter, eluting with an ethyl acetate/cyclohexane mixture (5/95 by volume) and collecting 15 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 1.00 g of 4α-butanoyloxy-1β,2α-carbonato-7β,13α-ditriethylsilyloxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-11-taxene is obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : from 0.50 to 0.70 (mt, 12H : CH_2 of the ethyl); 0.90 and 1.10 (mt, 21H : CH_3 of the ethyl and CH_3 of the propyl); 1.18 (s, 3H : CH_3); 1.28 (s, 3H : CH_3); 1.73 (mt, 2H : CH_2 of the propyl); 1.75 (s, 3H : CH_3); 1.92 and 2.59 (2 mts, 1H each : CH_2 at 6); 2.13 (s, 3H : CH_3); 2.14 and from 2.35 to 2.45 (dd and mt respectively, J = 16 and 9 Hz, 1H each : CH_2 at 14); from 2.35 to 2.45 (mt, 2H : $OCOCH_2$ of the propyl); 3.42 (d, J = 6.5 Hz, 1H : H at 3); 3.51 (s, 3H : OCH_3); 4.18 (s, 2H : $OCOCH_2O$); 4.46 (dd, J = 10 and 6.5 Hz, 1H : H at 7); 4,50 and 4.63 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.51 (d, J = 6.5 Hz, 1H : H at 2); 4.93 (broad d, J = 10 Hz, 1H : H at 5); 5.02 (broad t, J = 9 Hz, 1H : H at 13); 6.51 (s, 1H : H at 10).

EXAMPLE 4

By performing the process as in Example 3, and starting with 2α-benzoyloxy-4α-phenylacetoxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3 phenylpropionate, 2α-benzoyloxy-5β-20-epoxy-1β-hydroxy-10β-methoxyacetoxy-7β,8-methylene-19-nor-9-oxo-4α-phenylacetoxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate is obtained, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 1.24 (s,

15H : CH_3 - CH_3 and $C(CH_3)_3$); 1.40 (mt, 1H: H at 7); 1.66 and 2.24 (2 dd, J = 6 and 5 Hz and J = 10 and 6 Hz, 1H each : CH_2 at 19); 1.92 (s, 1H : OH at 1); 1.96 (s, 3H : CH_3); 2.07 and 2.46 (broad d and dt respectively, J = 16 Hz and J = 16 and 4.5 Hz, 1H each : CH_2 at 6); 2.32 and 2.54 (dd and broad dd respectively, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.24 (mt, 1H : OH at 2'); 3.53 (s, 3H : OCH_3); 3.90 and 4.14 (2 d, J = 15 Hz, 1H each : $OCOCH_2Ar$); 4.00 and 4.16 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.20 and 4.26 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.23 (d, J = 7 Hz, 1H : H at 3); 4.55 (broad d, J = 4.5 Hz, 1H : H at 5); 4,63 (mt, 1 H : H at 2'); 5.31 (limiting AB, 2H : H at 3' and CONH); 5.71 (d, J = 7 Hz, 1H : H at 2); 6.34 (broad t, J = 9 Hz, 1H : H at 13); 6.44 (s, 1H : H at 10); from 7.10 to 7.45 (mt, 10 H : aromatic H and aromatic H at 3'); 7.51 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.63 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.16 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-phenylacetoxy-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate is prepared, the characteristics of which are as follows:

- ^{1}H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 1.24 (s, 6H : CH_3); 1.36 (s, 9H : $C(CH_3)_3$); 1.74 (s, 1H, OH at 1); 1.87 (s, 3H : CH_3); 2.14 (s, 3H : CH_3); 2.19 and 2.83 (2 mts, 1H each : CH_2 at 6); 2.39 and 2.48 (2 broad dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.38 (d, J = 4.5 Hz, 1H : OH at 2'); 3.53 (s, 3H : OCH_3); 3.90 and 4.14 (2 d, J = 15 Hz, 1H each : $OCOCH_2Ar$); 4.01 (d, J = 7 Hz, 1H : H at 3); 4.11 and 4.20 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.17 and 4.25 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.65 (mt, 1H : H at 2'); 4,68 (broad d, J = 10 Hz, 1 H : H at 5); 5.28 (broad d, J = 10 Hz, 1H : H at 3'); 5.35 (d, J = 10 Hz, 1H : CONH); 5.50 (dd, J = 10 and 7 Hz, 1H : H at 7); 5.77 (d, J = 7 Hz, 1H : H at 2); 6.28 (broad t, J = 9 Hz, 1H : H at 13); 6.74 (s, 1H : H at 10); from 7.15 to 7.45 (mt, 10 H : aromatic H and aromatic H at 3'); 7.51 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.66 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.08 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-phenylacetoxy-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate is prepared, the characteristics of which are as follows:

- ^{1}H NMR spectrum (400 MHz; $CDCl_3$; a temperature of 333° K, δ in ppm) : 1.06 (s, 9H : $CH_3)_3$); 1.12 (s, 3H :

CH_3); 1.24 (s, 3H : CH_3); 1.66 (s, 1H : OH at 1); 1.83 (s, 3H : CH_3); 1.86 (s, 3H : CH_3); 2.14 and 2.79 (2 mts, 1H each : CH_2 at 6); 2.24 and 2.30 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.45 and 3.58 (2 d, J = 15 Hz, 1H each : $OCOCH_2Ar$); 3.54 (s, 3H : OCH_3); 3.85 (s, 3H : $ArOCH_3$); 3.94 (d, J = 7 Hz, 1H : H at 3); 4.08 and 4.17 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.14 and 4.22 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.59 (broad d, J = 10 Hz, 1H : H at 5); 4.63 (d, J = 5.5 Hz, 1H : H at 2'); 5.45 (d, J = 5.5 Hz, 1H : H at 3'); 5.47 (mt, 1H : H at 7); 5.72 (d, J = 7 Hz, 1H : H at 2); 6.14 (broad t, J = 9 Hz, 1H : H at 13); 6.34 (s, 1H : H at 5'); 6.65 (s, 1H : H at 10); 6.94 (d, J = 8.5 Hz, 2H : aromatic H ortho to the OCH_3); from 7.20 to 7.45 (mt, 12H : aromatic H and aromatic H meta to the OCH_3 and aromatic H at 3'); 7.48 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.64 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 7.98 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-1β,13α-dihydroxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-phenylacetoxy-7β-trifluoromethanesulphonyloxy-11-taxene is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 1.07 (s, 3H : CH_3); 1.21 (s, 3H: CH_3); 1.64 (s, 1H : OH at 1); 1.87 (s, 3H : CH_3); 2.18 (d, J = 4.5 Hz, 1H : OH at 13); 2.20 and 2.88 (2 mts, 1H each : CH_2 at 6); 2.30 (s, 3H :

CH_3); from 2.25 to 2.35 (mt, 2H : CH_2 at 14); 3.52 (s, 3H : OCH_3); 3.90 and 3.97 (2 d, J = 15 Hz, 1H each : $OCOCH_2Ar$); 4.08 (d, J = 7 Hz, 1H : H at 3); 4.12 and 4.27 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.16 and 4.24 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.80 (broad d, J = 10 Hz, 1H : H at 5); 4.92 (mt, 1H : H at 13); 5.55 (dd, J = 10 and 6.5 Hz, 1H : H at 7); 5.71 (d, J = 7 Hz, 1H : H at 2); 6.74 (s, 1H : H at 10); from 7.25 to 7.45 (mt, 5H : aromatic H); 7.48 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.64 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.03 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-phenylacetoxy-1β,7β,13α-trihydroxy-11-taxene is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 1.12 (s, 3H : CH_3); 1.14 (s, 3H: CH_3); 1.66 (s, 1H : OH at 1); 1.67 (s, 3H : CH_3); 1.84 and 2.56 (2 mts, 1H each : CH_2 at 6); 2.11 (s, 3H : CH_3); from 2.20 to 2.45 (2 mts, 1H each : OH); 2.35 and 2.42 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.54 (s, 3H : OCH_3); 3.94 (limiting AB, J = 15 Hz, 2H : $OCOCH_2Ar$); 3.94 (d, J = 7 Hz, 1H : H at 3); 4.12 and 4.25 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.26 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.50 (mt, 1H : H at 7); 4.87 (broad d, J = 10 Hz, 1H : H at 5); 4.96 (mt, 1H : H at 13); 5.66 (d, J = 7 Hz, 1H : H at 2); 6.44 (s, 1H : H at 10); from 7.25 to 7.45 (mt,

5H : aromatic H); 7.47 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.62 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.04 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-4α-phenylacetoxy-11-taxene is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 0.60 and 0.72 (2 mts, 6H each : CH_2 of the ethyl); 0.94 and 1.05 (2 t, J = 7.5 Hz, 9H each : CH_3 of the ethyl); 1.15 (s, 3H : CH_3); 1.22 (s, 3H: CH_3); 1.66 (s, 3H : CH_3); 1.69 (broad s, 1H : OH at 1); 1.84 and 2.51 (2 mts, 1H each : CH_2 at 6); 2.20 (s, 3H : CH_3); 2.24 and 2.36 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.54 (s, 3H : OCH_3); 3.82 and 3.96 (2 d, J = 15 Hz, 1H each : $OCOCH_2Ar$); 3.89 (d, J = 7 Hz, 1H : H at 3); 4.06 and 4.16 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.20 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.52 (dd, J = 10 and 6 Hz, 1H : H at 7); 4.79 (broad d, J = 10 Hz, 1H : H at 5); 4.96 (broad t, J = 9 Hz, 1H : H at 13); 5.66 (d, J = 7 Hz, 1H : H at 2); 6.58 (s, 1H : H at 10); from 7.25 to 7.45 (mt, 7H : aromatic H and $OCOC_6H_5$ meta-H); 7.61 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.00 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ at ortho-H).

By performing the process under similar conditions to those described in Example 3,

2α-benzoyloxy-1β,10β-dihydroxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-4α-phenylacetoxy-11-taxene is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (600 MHz; $CDCl_3$; δ in ppm) : 0.53 and 0.72 (2 mts, 6H each : CH_2 of the ethyl); 0.94 and 1.05 (2 t, J = 7.5 Hz, 9H each : CH_3 of the ethyl); 1.10 (s, 3H : CH_3); 1.20 (s, 3H: CH_3); 1.64 (s, 1H : OH at 1); 1.70 (s, 3H : CH_3); 1.86 and 2.45 (2 mts, 1H each : CH_2 at 6); 2.10 (s, 3H : CH_3); 2.20 and 2.32 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.80 and 3.96 (2 d, J = 16 Hz, 1H each : $OCOCH_2Ar$); 3.95 (d, J = 7 Hz, 1H : H at 3); 4.07 and 4.17 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.29 (broad s, 1H : OH at 10); 4.43 (dd, J = 11 and 7 Hz, 1H : H at 7); 4.79 (broad d, J = 10 Hz, 1H : H at 5); 5.03 (broad t, J = 9 Hz, 1H : H at 13); 5.19 (broad s, 1H : H at 10); 5.63 (d, J = 7 Hz, 1H : H at 2); from 7.25 to 7.45 (mt, 7H : aromatic H and $OCOC_6H_5$ meta-H); 7.60 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.00 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 1β,2α-carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-4α-phenylacetoxy-11-taxene is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 0.61 and 0.74 (2 mts, 6H each : CH_2 of the ethyl); 0.92 and 1.05 (2 t, J = 7.5 Hz, 9H each : CH_3 of the ethyl); 1.20 (s,

3H : CH_3); 1.30 (s, 3H: CH_3); 1.73 (s, 3H : CH_3); 1.83 and 2.54 (2 mts, 1H each : CH_2 at 6); 2.18 (s, 3H : CH_3); 2.27 and 2.48 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.50 (d, J = 6.5 Hz, 1H : H at 3); 3.53 (s, 3H : OCH_3); 3.65 (limiting AB, J = 14 Hz, 2H : $OCOCH_2Ar$); 4.18 (limiting AB, 2H : $OCOCH_2O$); 4.45 and 4.53 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.46 (mt, 1H : H at 7); 4.53 (d, J = 6.5 Hz, 1H : H at 2); 4.68 (broad d, J = 10 Hz, 1H : H at 5); 5.06 (broad t, J = 9 Hz, 1H : H at 13); 6.53 (s, 1H : H at 10); from 7.25 to 7.45 (mt, 5H : aromatic H).

EXAMPLE 5

By performing the process as in Example 3, and starting with 2α-benzoyloxy-4α,10β-bis(methoxyacetoxy)-5β,20-epoxy-1β,hydroxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate,2α-benzoyloxy-4α,10β-bis(methoxyacetoxy)-5β,20-epoxy-1β-hydroxy-7β,8-methylene-19-nor-9-oxo-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; temperature of 333° K, δ in ppm) : 1.26 (s, 3H : CH_3); 1.29 (s, 3H : CH_3); 1.35 (s, 9H : $C(CH_3)_3$); 1.42 (mt, 1H : H at 7); 1.71 and 2.29 (dd and mt respectively, J = 6.5 and 5 Hz, 1H each : CH_2 at 19); 1.81 (s, 1H : OH at 1); 1.91

(s, 3H : CH_3); 2.15 and 2.54 (broad d and dt respectively, J = 16 Hz and J = 16 and 4.5 Hz, 1H each : CH_2 at 6); 2.32 (limiting AB, 2H : CH_2 at 14); 3.50 and 3.53 (2 s, 3H each : OCH_3); 3.60 (mult. 1H, OH at 2'); 4.11 and 4.56 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.12 and 4.31 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.17 (d, J = 7 Hz, 1H : H at 3); 4.19 and 4.24 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.67 (mt, 1H : H at 2'); 4.78 (d, J = 4.5 Hz, 1H : H at 5); 5.29 (broad d, J = 10 Hz, 1H : H at 3'); 5.47 (d, J = 10 Hz, 1H : CONH); 5.70 (d, J = 7 Hz, 1H : H at 2); 6.21 (broad t, J = 9 Hz, 1H : H at 13); 6.44 (s, 1H : H at 10); 7.30 (t, J = 7.5 Hz, 1H : para-H of the aromatic at 3'); 7.39 (t, J = 7.5 Hz, 2H : meta-H of the aromatic at 3'); 7.45 (d, J = 7.5 Hz, 2H : ortho-H of the aromatic at 3'); 7.51 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.61 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.12 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-4α,10β-bis(methoxyacetoxy)-5β,20-epoxy-1β-hydroxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; temperature of 333° K, δ in ppm) : 1.22 (s, 3H : CH_3); 1.27 (s, 3H : CH_3); 1.38 (s, 9H : $C(CH_3)_3$); 1.64 (s, 1H : OH at 1);

1.92 (s, 3H : CH_3); 2.11 (s, 3H : CH_3); 2.25 and 2.92 (2 mts, 1H each : CH_2 at 6); 2.26 and 2.36 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.47 and 3.52 (2 s, 3H each : OCH_3); 3.66 (broad s, 1H, OH at 2'); 3.99 (d, J = 7 Hz, 1H : H at 3); 4.15 and 4.57 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.19 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.24 and 4.35 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.70 (mt, 1H : H at 2'); 4.95 (broad d, J = 10 Hz, 1H : H at 5); 5 29 (broad d, J = 10 Hz, 1H : H at 3'); 5.49 (d, J = 10 Hz, 1H : CONH); 5.53 (dd, J = 11 and 8 Hz, 1H : H at 7); 5.76 (d, J = 7 Hz, 1H : H at 2); 6.18 (broad t, J = 9 Hz, 1H : H at 13); 6.74 (s, 1H : H at 10); 7.30 (t, J = 7.5 Hz, 1H : para-H of the aromatic at 3'); 7.38 (t, J = 7.5 Hz, 2H : meta-H of the aromatic at 3'); 7.45 (d, J = 7.5 Hz, 2H : ortho-H of the aromatic at 3'); 7.49 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.63 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.09 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-4α,10β-bis(methoxyacetoxy)-5β,20-epoxy-1β-hydroxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; temperature of 333° K, δ in ppm) : 1.10 (s, 9H : $(CCH_3)_3$); 1.18 (s, 3H

: CH_3); 1.20 (s, 3H : CH_3); 1.64 (s, 1H : OH at 1); 1.75 (s, 3H : CH_3); 1.86 (s, 3H : CH_3); 2.12 and 2.26 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 2.24 and 2.86 (2 mts, 1H each : CH_2 at 6); 3.33 and 3.53 (2 s, 3H : OCH_3); 3.65 and 4.10 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 3.83 (s, 3H: $ArOCH_3$); 3.86 (d, J = 7 Hz, 1H : H at 3); 4.14 and 4.20 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.19 and 4.32 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.72 (broad d, J = 4.5 Hz, 1H : H at 2'); 4.89 (broad d, J = 10 Hz, 1H : H at 5); 5 46 (mt, 1H : H at 3'); 5.45 (dd, J = 11 and 8 Hz, 1H : H at 7); 5.69 (d, J = 7 Hz, 1H : H at 2); 5.94 (broad t, J = 9 Hz, 1H : H at 13); 6.40 (broad s, 1H : H at 5'); 6.63 (s, 1H : H at 10); 6.93 (d, J = 8.5 Hz, 2H : aromatic ortho-H at OCH_3); from 7.30 to 7.45 (mt, 5H : aromatic H at 3'); 7.38 (d, J = 8.5 Hz, 2H : aromatic meta-H at OCH_3); 7.48 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.63 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.08 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-4α,10β-bis(methoxyacetoxy)-1β,13α-dihydroxy-5β,20-epoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxene is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 1.06 (s, 3H : CH_3); 1.20 (s, 3H : CH_3); 1.61 (s, 1H : OH at 1); 1.89 (s, 3H : CH_3); 2.23 (d, J = 5 Hz, 1H : OH at 13);

from 2.20 to 2.35 and 2.92 (2 mts, 1H each : CH_2 at 6); 2.26 (s, 3H : CH_3); 2.32 (d, J = 9 Hz, 2H : CH_2 at 14); 3.52 and 3.58 (2s, 3H each : OCH_3); 4.04 (d, J = 7 Hz, 1H : H at 3); 4.19 and 4.32 (2 limiting AB, J = 16 Hz, 2H each : $OCOCH_2O$); 4.20 and 4.38 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.82 (mt, 1H : H at 13); 4.99 (broad d, J = 10 Hz, 1H : H at 5); 5.55 (d, J = 10 and 7 Hz, 1H : H at 7); 5.69 (d, J = 7 Hz, 1H : H at 2); 6.73 (s, 1H : H at 10); 7.51 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.64 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.13 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-4α,10β-bis(methoxyacetoxy)-5β,20-epoxy-9-oxo-1β,7β,13α-trihydroxy-11-taxene is prepared, the characteristics of which are as follows:

- ^{1}H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 1.11 (s, 6H : CH_3); 1.63 (s, 1H : CH at 1); 1.70 (s, 3H : CH_3); 1.92 and 2.63 (2 mts, 1H each : CH_2 at 6); 2.08 (s, 3H : CH_3); from 2.20 to 2.30 (mt, 3H : CH_2 at 14 and OH); 2.40 (d, J = 4 Hz, 1H : OH); 3.54 and 3.59 (2 s, 3H each : OCH_3); 3.92 (d, J = 7 Hz, 1H : H at 3); 4.20 and 4.35 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.24 and 4.28 (2 limiting AB, J = 16 Hz, 2H each : $OCOCH_2O$); 4.50 (mt, 1H : H at 7); 4.86 (mt, 1H : H at 13); 5.03 (broad d, J = 10 Hz, 1H : H at 5); 5.65 (d, J = 7 Hz, 1H : H at 2); 6.44 (s, 1H : H at 10); 7.49 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.63 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$

para-H); 8.14 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-4α,10β-bis(methoxyacetoxy)-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-1β-hydroxy-9-oxo-11-taxene is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 0.60 and 0.70 (2 mts, 6H each : CH_2 of the ethyl); 0.94 and 1.02 (2 t, J = 7.5 Hz, 9H each : CH_3 of the ethyl); 1.12 (s, 3H : CH_3); 1.20 (s, 3H : CH_3); 1.64 (s, 1H : OH at 1); 1.70 (s, 3H : CH_3); 1.91 and 2.57 (2 mts, 1H each : CH_2 at 6); 2.12 (s, 3H : CH_3); 2.13 and 2.23 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.53 and 3.57 (2 s, 3H each : OCH_3); 3.83 (d, J = 7 Hz, 1H : H at 3); 4.15 and 4.40 (2 d, J = 16 Hz, 2H : $OCOCH_2O$); 4.19 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.21 and 4.37 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.51 (dd, J = 11 and 7 Hz, 1H : H at 7); 4.93 (t, J = 9 Hz, 1H : H at 13); 5.02 (broad d, J = 10 Hz, 1H : H at 5); 5.64 (d, J = 7 Hz, 1H : H at 2); 6.56 (s, 1H : H at 10); 7.48 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.63 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.19 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-1β,10β-dihydroxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-4α-methoxyacetoxy-9-oxo-11-taxene is prepared, the characteristics of which

are as follows:

- ^{1}H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 0.57 and 0.69 (2 mts, 6H each : CH_2 of the ethyl); 0.94 and 1.03 (2 t, J = 7.5 Hz, 9H each : CH_3 of the ethyl); 1.09 (s, 3H : CH_3); 1.17 (s, 3H : CH_3); 1.58 (s, 1H : OH at 1); 1.75 (s, 3H : CH_3); 1.93 and 2.49 (2 mts, 1H each : CH_2 at 6); 2.03 (s, 3H : CH_3); 2.09 and 2.18 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.57 (s, 3H : OCH_3); 3.88 (d, J = 7 Hz, 1H : H at 3); 4.16 and 4.40 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.20 and 4.36 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.28 (broad s, 1H : OH at 10); 4.42 (mt, 1H : H at 7); 4.97 (t, J = 9 Hz, 1H : H at 13); 5.01 (broad d, J = 10 Hz, 1H : H at 5); 5.17 (broad s, 1H : H at 10); 5.62 (d, J = 7 Hz, 1H : H at 2); 7.47 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.61 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.18 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 4α,10β-bis(methoxyacetoxy)-1β,2α-carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-11-taxene is prepared, the characteristics of which are as follows:

- ^{1}H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm) : 0.60 and 0.68 (2 mts, 6H each : CH_2 of the ethyl); 0.92 and 1.01 (2 t, J = 7.5 Hz, 9H each : CH_3 of the ethyl); 1.19 (s, 3H : CH_3); 1.27 (s, 3H : CH_3); 1.75 (s, 3H : CH_3); 1.91 and 2.63 (2 mts, 1H each : CH_2 at 6); 2.08 and 2.41 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 2.12 (s,

3H : CH_3); 3.44 (d, J = 6.5 Hz, 1H : H at 3); 3.46 and 3.50 (2 s, 3H each : OCH_3); 4.06 and 4.14 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.16 (s, 2H : $OCOCH_2O$); 4.46 (dd, J = 10 and 7 Hz, 1H : H at 7); 4.50 and 4.66 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.51 (d, J = 6.5 Hz, 1H : H at 2); 4.99 (mt, 1H : H at 13); 5.00 (broad d, J = 10 Hz, 1H : H at 5); 6.51 (s, 1H : H at 10).

EXAMPLE 6

By performing the process as in Example 3, and starting with 2α-benzoyloxy-4α-cyclopropanoyloxy-5β,20-epoxy-1β-hydroxy-9-oxo-10β-methoxyacetoxy-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate, 2α-benzoyloxy-4α-cyclopropanoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-7β,8-methylene-19-nor-9-oxo-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; temperature in the region of 333° K, δ in ppm): from 0.80 to 1.40 (mt, 4H : CH_2CH_2 of the cyclopropyl); 1.30 (s, 6H : CH_3); 1.35 (s, 9H : $C(CH_3)_3$); from 1.30 to 1.40 (mt, 1H : H at 7); 1.70 and 2.23 (2 dd, J = 6 and 5.5 Hz and J = 10 and 5.5 Hz respectively, 1H each : CH_2 at 19); 1.80 (mt, 1H : CH of the cyclopropyl); 1.85 (s, 1H : OH at 1); 1.86 (s, 3H : CH_3); 2.11 and 2.44 (broad d and dt respectively, J = 16 Hz and J = 16 and 4.5 Hz, 1H

each : CH_2 at 6); 2.34 and 2.50 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.22 (d, J = 4 Hz, 1H : OH at 2'); 3.52 (s, 3H : OCH_3); 4.08 and 4.28 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.13 (d, J = 7 Hz, 1H : H at 3); 4.16 and 4.24 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.62 (d, J = 4.5 Hz, 1H : H at 5); 4.70 (broad d, J = 4 Hz, 1H : H at 2'); 5.28 (limiting AB, 2H : H3' and CONH); 5.70 (d, J = 7 Hz, 1H : H at 2); 6.23 (broad t, J = 9 Hz, 1H : H at 13); 6.42 (s, 1H : H at 10); from 7.20 to 7.45 (mt, 5H : aromatic H at 3'); 7.52 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.61 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.14 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-4α-cyclopropanoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,3S)-3-tert-butoxycarbonylamino-2-hydroxy-3-phenylpropionate is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm): from 0.85 to 1.40 (mt, 4H : CH_2CH_2 of the cyclopropyl); 1.22 (s, 3H : CH_3); 1.24 (s, 3H : CH_3); 1.39 (s, 9H: $C(CH_3)_3$); 1.70 (s, 1H : OH at 1); 1.83 (mt, 1H : CH of the cyclopropyl); 1.88 (s, 3H : CH_3); 2.05 (s, 3H : CH_3); 2.23 and 2.84 (2 mts, 1H each : CH_2 at 6); 2.34 and 2.42 (2 dd, J = 16 and 9 Hz, 1H each: CH_2 at 14); 3.35 (d, J = 5.5 Hz, 1H : OH at 2'); 3.52 (s, 3H : OCH_3); 3.96

(d, J = 7 Hz, 1H : H at 3); 4.16 and 4.25 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.17 and 4.28 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.72 (mt, 1H : H at 2'); 4.81 (broad d, J = 10 Hz, 1H : H at 5); 5.28 (broad d, J = 10 Hz, 1H : H at 3'); 5.36 (d, J = 10 Hz, 1H : CONH); 5.48 (dd, J = 10.5 and 7 Hz, 1H : H at 7); 5.72 (d, J = 7 Hz, 1H : H at 2); 6.11 (mt, 1H : H at 13); 6.71 (s, 1H : H at 10); from 7.25 to 7.45 (mt, 5H : aromatic H at 3'); 7.52 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.65 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.08 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-4α-cyclopropanoyloxy-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxen-13α-yl (2R,4S,5R)-3-tert-butoxycarbonyl-2-(4-methoxyphenyl)-4-phenyl-1,3-oxazolidine-5-carboxylate is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm): from 0.50 to 1.50 (mt, 5H : CH and CH_2 of the cyclopropyl); 1.04 (s, 9H : $C(CH_3)_3$); 1.17 (s, 3H : CH_3); 1.19 (s, 3H : CH_3); 1.65 (s, 1H : OH at 1); 1.72 (s, 3H : CH_3); 1.84 (s, 3H : CH_3); 2.14 and 2.32 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 2.16 and 2.79 (2 mts, 1H each : CH_2 at 6); 3.52 (s, 3H : OCH_3); 3.82 (s, 3H : $ArOCH_3$); 3.86 (d, J = 7 Hz, 1H : H at 3); 4.11 and 4.24 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.15 and 4.22 (2 d, J =

16 Hz, 1H each : $OCOCH_2O$); 4.60 (d, J = 4.5 Hz, 1H : H at 2'); 4.74 (broad d, J = 10 Hz, 1H : H at 5); 5.44 (dd, J = 10.5 and 8 Hz, 1H : H at 7); 5.50 (mt, 1H : H at 3'); 5.67 (d, J = 7 Hz, 1H : H at 2); 5.88 (mt, 1H : H at 13); 6.41 (mult., 1H : H at 5'); 6.61 (s, 1H : H at 10); 6.92 (d, J = 8.5 Hz, 2H : aromatic H ortho to the OCH_3) 7.38 (d, J = 8.5 Hz, 2H : aromatic H meta to the OCH_3); from 7.25 to 7.45 (mt, 5H : aromatic H at 3'); 7.49 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.63 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.02 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-4α-cyclopropanoyloxy-1β,13α-dihydroxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxene is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; temperature of 333° K, δ in ppm): from 0.90 to 1.40 (mt, 4H : CH_2CH_2 of the cyclopropyl); 1.10 (s, 3H : CH_3); 1.22 (s, 3H : CH_3); 1.61 (s, 1H : OH at 1); from 1.70 to 1.85 (mt, 2H: CH of the cyclopropyl and OH at 13); 1.90 (s, 3H : CH_3); 2.22 and 2.86 (2 mts, 1H each : CH_2 at 6); 2.26 (s, 3H : CH_3); 2.36 (d, J = 9 Hz, 2H : CH_2 at 14); 3.52 (s, 3H : OCH_3); 4.05 (d, J = 7 Hz, 1H : H at 3); 4.14 and 4.22 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.20 and 4.36 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.84 (mt, 1H : H at 13); 4.85 (broad d, J = 10 Hz, 1H : H at 5); 5.54 (dd,

J = 11 and 8 Hz, 1H : H at 7); 5.72 (d, J = 7 Hz, 1H : H at 2); 6.73 (s, 1H : H at 10); 7.51 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.63 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.12 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-4α-cyclopropanoyloxy-1β,13α-dihydroxy-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-7β-trifluoromethanesulphonyloxy-11-taxene is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; temperature of 333° K, δ in ppm): from 0.90 to 1.40 (mt, 4H : CH_2CH_2 of the cyclopropyl); 1.10 (s, 3H : CH_3); 1.22 (s, 3H : CH_3); 1.61 (s, 1H : OH at 1); from 1.70 to 1.85 (mt, 2H : CH of the cyclopropyl and OH at 13); 1.90 (s, 3H : CH_3); 2.22 and 2.86 (2 mts, 1H each : CH_2 at 6); 2.26 (s, 3H : CH_3); 2.36 (d, J = 9 Hz, 2H : CH_2 at 14); 3.52 (s, 3H : OCH_3); 4.05 (d, J = 7 Hz, 1H : H at 3); 4.14 and 4.22 (2 d, J = 16 Hz, 1H each : $OCOCH_2O$); 4.20 and 4.36 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.84 (mt, 1H : H at 13); 4.85 (broad d, J = 10 Hz, 1H : H at 5); 5.54 (dd, J = 11 and 8 Hz, 1H : H at 7); 5.72 (d, J = 7 Hz, 1H : H at 2); 6.73 (s, 1H : H at 10); 7.51 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.63 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.12 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3,

2α-benzoyloxy-4α-cyclopropanoyloxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-1β-hydroxy-10β-methoxyacetoxy-9-oxo-11-taxene is prepared, the characteristics of which are as follows:

- ^{1}H NMR spectrum (400 MHz; $CDCl_3$, δ in ppm): 0.60 and 0.68 (2 mts, 6H each : CH_2 of the ethyl); from 0.90 to 1.35 (mt, 4H : CH_2CH_2 of the cyclopropyl); 0.94 and 1.03 (2 t, J = 7.5 Hz, 9 H each : CH_3 of the ethyl); 1.14 (s, 3H : CH_3); 1.20 (s, 3H : CH_3); 1.64 (s, 1H : OH at 1); 1.71 (s, 3H : CH_3); 1.73 (mt, 1H : CH of the cyclopropyl); 1.87 and 2.50 (broad dd and mt respectively; J = 14 and 11 Hz, 1H each : CH_2 at 6); 2.11 and 2.29 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 2.15 (s, 3H : CH_3); 3.53 (s, 3H : OCH_3); 3.86 (d, J = 7 Hz, 1H : H at 3); 4.14 and 4.26 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.19 (limiting AB, J = 16 Hz, 2H : $OCOCH_2O$); 4.52 (dd, J = 11 and 7 Hz, 1H : H at 7); 4.84 (broad d, J = 10 Hz, 1H : H at 5); 4.95 (broad t, J = 9 Hz, 1H : H at 13); 5.65 (d, J = 7 Hz, 1H : H at 2); 6.56 (s, 1H : H at 10); 7.50 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.62 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.09 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

By performing the process under similar conditions to those described in Example 3, 2α-benzoyloxy-4α-cyclopropanoyloxy-1β,10β-dihydroxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-9-oxo-11-taxene is prepared, the characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$, δ in ppm); 0.58 and 0.68 (2 mts, 6H each : CH_2 of the ethyl); from 0.90 to 1.35 (mt, 4H : CH_2CH_2 of the cyclopropyl); 0.94 and 1.03 (2 t, J = 7.5 Hz, 9H each : CH_3 of the ethyl); 1.12 (s, 3H : CH_3); 1.22 (s, 3H : CH_3); 1.59 (s, 1H : OH at 1); 1.67 (mt, 1H : CH of the cyclopropyl); 1.73 (s, 3H : CH_3); 1.90 and 2.44 (2 mts, 1H each : CH_2 at 6); 2.06 (s, 3H : CH_3); 2.10 and 2.25 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.91 (d, J = 7 Hz, 1H : H at 3); 4.16 and 4.26 (2 d, J = 9 Hz, 1H each : CH_2 at 20); 4.28 (d, J = 1.5 Hz, 1H : OH at 10); 4.42 (dd, J = 11 and 6 Hz, 1H : H at 7); 4.84 (broad d, J = 10 Hz, 1H : H at 5); 5.00 (t, J = 9 Hz, 1H : H at 13); 5.16 (d, J = 1.5 Hz, 1H : H at 10); 5.62 (d, J = 7 Hz, 1H : H at 2); 7.50 (t, J = 7.5 Hz, 2H : $OCOC_6H_5$ meta-H); 7.62 (t, J = 7.5 Hz, 1H : $OCOC_6H_5$ para-H); 8.09 (d, J = 7.5 Hz, 2H : $OCOC_6H_5$ ortho-H).

1β,2α-Carbonato-4α-cyclopropanoyloxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-11-taxene may be prepared in the following way:

To a solution of 100 mg of 1β,2α-carbonato-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-4α-hydroxy-10β-methoxyacetoxy-9-oxo-11-taxene in 7 cm^3 of tetrahydrofuran are added dropwise, at a temperature in the region of -30°C, 345 μl of a 1M solution of lithium hexamethyldisilazane in hexane. The reaction mixture is stirred for 15 minutes at this temperature, followed by dropwise addition of 39 μl of cyclopropanoyl chloride.

The reaction mixture is stirred for 30 minutes at a temperature in the region of 0°C, followed by hydrolysis by addition of 1 cm^3 of saturated ammonium chloride solution and 50 cm^3 of dichloromethane. The organic phase is separated out after settling of the phases has taken place, washed with twice 40 cm^3 of saturated aqueous sodium chloride solution and then dried over magnesium sulphate, filtered and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 120 mg of a product are obtained, which product is purified by chromatography on 70 g of silica (0.063-0.2 mm) contained in a column 2 cm in diameter, eluting with an ethyl acetate/cyclohexane mixture (20/80 by volume) and collecting 10 cm^3 fractions. The fractions containing only the desired product are combined and concentrated to dryness under reduced pressure (2.7 kPa) at 40°C. 31 mg of 1β,2α-carbonato-4α-cyclopropanoyloxy-7β,13α-bis(triethylsilyloxy)-5β,20-epoxy-10β-methoxyacetoxy-9-oxo-11-taxene are obtained in the form of a white foam, the physical characteristics of which are as follows:

- ^1H NMR spectrum (400 MHz; $CDCl_3$; δ in ppm): 0.60 and 0.66 (2 mts, 6H each : CH_2 of the ethyl); from 0.90 to 1.35 (mt, 4H : CH_2CH_2 of the cyclopropyl); 0.92 and 1.02 (2 t, J = 7.5 Hz, 9H each : CH_3 of the ethyl); 1.19 (s, 3H : CH_3); 1.29 (s, 3H : CH_3); 1.60 (s, 1H : OH at 1); 1.62 (mt, 1H : CH of the cyclopropyl); 1.73 (s, 3H : CH_3); 1.88 and 2.57 (broad dd and mt respectively, J =

15 and 10 Hz, 1H each : CH_2 at 6); 2.15 (s, 3H : CH_3); 2.19 and 2.37 (2 dd, J = 16 and 9 Hz, 1H each : CH_2 at 14); 3.48 (d, J = 7 Hz, 1H : H at 3); 3.51 (s, 3H : OCH_3); 4.16 (s, 2H : $OCOCH_2O$); 4.44 (mt, 1H : H at 7); 4.45 and 4.54 (2 d, J = 9 Hz, 1h each : CH_2 at 20); 4.49 (d, J = 7 Hz, 1H : H at 2); 4.85 (broad d, J = 10 Hz, 1H : H at 5); 5.02 (broad t, J = 9 Hz, 1H : H at 13); 6.52 (s, 1H : H at 10).

The novel products of general formula (I) in which Z represents a radical of general formula (II) exhibit significant inhibitory activity on abnormal cell proliferation and possess therapeutic properties which make it possible to treat patients having pathological conditions associated with abnormal cell proliferation. The pathological conditions include the abnormal cell proliferation of malignant or benign cells of various tissues and/or organs comprising, without any limitation being implied, muscle, bone or conjunctive tissues, the skin, the brain, the lungs, the sexual organs, the lymphatic or renal systems, breast or blood cells, the liver, the digestive system, the pancreas and the thyroid or adrenal glands. These pathological conditions may also include psoriasis, solid tumours, cancers of the ovary, breast, brain, prostate, colon, stomach, kidney or testicles, Kaposi's sarcoma, cholangiocarcinoma, choriocarcinoma, neuroblastoma, Wilms' tumour, Hodgkin's disease, melanomas, multiple myelomas, chronic lymphocytic

leukaemias and acute or chronic granulocytic lymphomas. The novel products according to the invention are particularly useful for treating cancer of the ovary. The products according to the invention may be used for preventing or delaying the appearance or reappearance of the pathological conditions or for treating these pathological conditions.

The products according to the invention may be administered to a patient in various forms adapted to the chosen route of administration, which is preferably the parenteral route. Administration via the parenteral route comprises intravenous, intraperitoneal, intramuscular or subcutaneous administrations. Intraperitoneal or intravenous administration is more particularly preferred.

The present invention also comprises the pharmaceutical compositions which contain at least one product of general formula (I) in a sufficient amount suitable for use in human or veterinary therapy. The compositions may be prepared according to the usual methods, using one or more pharmaceutically acceptable adjuvants, vehicles or excipients. Suitable vehicles include diluents, sterile aqueous media and various non-toxic solvents. The compositions are preferably provided in the form of aqueous solutions or suspensions, of injectable solutions which may contain emulsifying agents, dyes, preserving agents or stabilizing agents.

The choice of adjuvants or excipients may be determined by the solubility and the chemical properties of the product, the particular mode of administration and good pharmaceutical practice.

Aqueous or non-aqueous sterile solutions or suspensions are used for parenteral administration. For the preparation of non-aqueous solutions or suspensions, natural vegetable oils such as olive oil, sesame oil or liquid paraffin, or injectable organic esters such as ethyl oleate, may be used. The aqueous sterile solutions may consist of a solution of a pharmaceutically acceptable salt dissolved in water. The aqueous solutions are suitable for intravenous administration provided that the pH is appropriately adjusted and that the solution is made isotonic, for example with a sufficient amount of sodium chloride or glucose. The sterilization may be performed by heating or by any other means which does not adversely affect the composition.

It is clearly understood that all the products entering into the compositions according to the invention must be pure and non-toxic in the amounts used.

The compositions may contain at least 0.01 % of therapeutically active product. The amount of active product in a composition is such that a suitable dosage may be prescribed. The compositions are preferably prepared such that a single dose contains from 0.01 to

1000 mg approximately of active product for administration via the parenteral route.

The therapeutic treatment may be carried out concurrently with other therapeutic treatments including antineoplastic drugs, monoclonal antibodies, immunotherapies or radiotherapies or biological-response modifiers. The response modifiers include, without any limitation being implied, lymphokines and cytokines such as interleukins, interferons (α, β or δ) and TNF. Other chemotherapeutic agents which are useful in the treatment of disorders due to abnormal cell proliferation include, without any limitation being implied, alkylating agents such as nitrogen mustards, for instance mechloretamine, cyclophosphamide, melphalan and chlorambucil, alkyl sulphonates, for instance busulphan, nitrosoureas, for instance carmustine, lomustine, semustine and streptozocin, triazenes, for instance dacarbazine, antimetabolites, for instance folic acid analogues such as methotrexate, pyrimidine analogues, for instance fluorouracil and cytarabine, purine analogues, for instance mercaptopurine and thioguanine, natural products such as vinca alkaloids, for instance vinblastine, vincristine and vendesine, epipodophyllotoxins, for instance etoposide and teniposide, antibiotics, for instance dactinomycin, daunorubicin, doxorubicin, bleomycin, plicamycin and mitomycin, enzymes, for instance L-asparaginase, various agents, for instance

platinum coordination complexes such as cisplatin, substituted ureas such as hydroxyurea, methylhydrazine derivatives, for instance procarbazine, adrenocorticoid suppressants, for instance mitotane and aminoglutethymide, hormones and antagonists, for instance adrenocorticosteroids, for instance prednisone, progestins, for instance hydroxyprogesterone caproate, methoxyprogesterone acetate and megestrol acetate, oestrogens, for instance diethylstilbestrol and ethynylestradiol, antioestrogens such as tamoxifen, and androgens, for instance testosterone propionate and fluoxymesterone.

The doses used for implementing the methods according to the invention are those which permit a prophylactic treatment or a maximum therapeutic response. The doses vary according to the form of administration, the particular product selected and the personal characteristics of the subject to be treated. In general, the doses are those which are therapeutically effective for the treatment of disorders due to abnormal cell proliferation. The products according to the invention may be administered as often as necessary in order to obtain the desired therapeutic effect. Some patients may respond rapidly to relatively high or low doses, and then require low or zero maintenance doses. Generally, low doses will be used at the start of the treatment and, if necessary, increasingly high doses will be administered until an

optimum effect is obtained. For other patients, it may be necessary to administer maintenance doses 1 to 8 times a day, preferably 1 to 4 times, according to the physiological needs of the patient in question. It is also possible that, for certain patients, only one to two daily administrations are necessary.

In man, the doses are generally between 0.01 and 200 mg/kg. Via the intraperitoneal route, the doses will generally be between 0.1 and 100 mg/kg and preferably between 0.5 and 50 mg/kg and even more specifically between 1 and 10 mg/kg. Via the intravenous route, the doses will generally be between 0.1 and 50 mg/kg and preferably between 0.1 and 5 mg/kg and even more specifically between 1 and 2 mg/kg. It is understood that, in order to choose the most suitable dosage, the route of administration, the patient's weight, general state of health and age, and all the factors which may influence the effectiveness of the treatment, will have to be taken into account.

The example which follows illustrates a composition according to the invention.

EXAMPLE

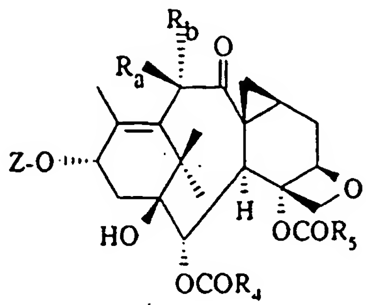
40 mg of the product obtained in Example 1 are dissolved in 1 cm^3 of Emulphor EL 620 and 1 cm^3 of ethanol, and the solution is then diluted by addition of 18 cm^3 of physiological serum.

The composition is administered by infusion over 1 hour by introduction into physiological

solution.

CLAIMS

1. Novel taxoids of general formula:

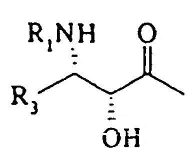


(I)

in which:

R_a represents a hydrogen atom or a hydroxyl radical, an alkoxy radical containing 1 to 4 carbon atoms, an acyloxy radical containing 1 to 4 carbon atoms or an alkoxyacetoxy radical in which the alkyl part contains 1 to 4 carbon atoms and R_b represents a hydrogen atom, or alternatively R_a and R_b form, together with the carbon atom to which they are attached, a ketone function,

Z represents a hydrogen atom or a radical of general formula:



(II)

in which:

R_1 represents a benzoyl radical optionally substituted with one or more atoms or radicals, which may be identical or different, chosen from halogen

atoms and alkyl radicals containing 1 to 4 carbon atoms, alkoxy radicals containing 1 to 4 carbon atoms, trifluoromethyl, thenoyl and furoyl radicals, or a radical R_2-O-CO- in which R_2 represents:

- an alkyl radical containing 1 to 8 carbon atoms, an alkenyl radical containing 2 to 8 carbon atoms, an alkynyl radical containing 3 to 8 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a cycloalkenyl radical containing 4 to 6 carbon atoms, or a bicycloalkyl radical containing 7 to 10 carbon atoms, these radicals being optionally substituted with one or more substituents chosen from halogen atoms and hydroxyl radicals, alkoxy radicals containing 1 to 4 carbon atoms, dialkylamino radicals in which each alkyl part contains 1 to 4 carbon atoms, piperidino and morpholino radicals, 1-piperazinyl radicals (optionally substituted at -4 with an alkyl radical containing 1 to 4 carbon atoms or with a phenylalkyl radical in which the alkyl part contains 1 to 4 carbon atoms), cycloalkyl radicals containing 3 to 6 carbon atoms, cycloalkenyl radicals containing 4 to 6 carbon atoms, phenyl radicals (optionally substituted with one or more atoms or radicals chosen from halogen atoms and alkyl radicals containing 1 to 4 carbon atoms or alkoxy radicals containing 1 to 4 carbon atoms), cyano or carboxyl radicals and alkoxycarbonyl radicals in which the alkyl part contains 1 to 4 carbon atoms,
- a phenyl or α- or β-napthyl radical which is

optionally substituted with one or more atoms or radicals chosen from halogen atoms and alkyl radicals containing 1 to 4 carbon atoms or alkoxy radicals containing 1 to 4 carbon atoms or a 5-membered aromatic heterocyclic radical preferably chosen from furyl and thienyl radicals,

- or a saturated heterocyclic radical containing 4 to 6 carbon atoms optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms,

R_3 represents a straight or branched alkyl radical containing 1 to 8 carbon atoms, a straight or branched alkenyl radical containing 2 to 8 carbon atoms, a straight or branched alkynyl radical containing 2 to 8 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, or a phenyl or α- or β-naphthyl radical which is optionally substituted with one or more atoms or radicals chosen from halogen atoms and alkyl, alkenyl, alkynyl, aryl, aralkyl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxyalkyl, mercapto, formyl, acyl, acylamino, aroylamino, alkoxycarbonylamino, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, cyano, nitro and trifluoromethyl radicals, or a 5-membered aromatic heterocycle containing one or more hetero atoms, which may be identical or different, chosen from nitrogen, oxygen and sulphur atoms and optionally substituted with one or more substituents, which may be identical or

different, chosen from halogen atoms, and alkyl, aryl, amino, alkylamino, dialkylamino, alkoxycarbonylamino, acyl, arylcarbonyl, cyano, carboxyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl and alkoxycarbonyl radicals, it being understood that, in the substituents of the phenyl, α- or β-naphthyl and aromatic heterocyclic radicals, the alkyl radicals and the alkyl portions of the other radicals contain 1 to 4 carbon atoms and that the alkenyl and alkynyl radicals contain 2 to 8 carbon atoms and that the aryl radicals are phenyl or α- or β-naphthyl radicals, and

R_4 and R_5, which may be identical or different, represent

- a straight or branched alkyl radical containing 1 to 8 carbon atoms, a straight or branched alkenyl radical containing 2 to 8 carbon atoms, a straight or branched alkynyl radical containing 2 to 8 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a cycloalkenyl radical containing 4 to 6 carbon atoms or a bicycloalkyl radical containing 7 to 11 carbon atoms, these radicals optionally being substituted with one or more substituents chosen from halogen atoms and hydroxyl radicals, alkyloxy radicals containing 1 to 4 carbon atoms, dialkylamino radicals in which each alkyl part contains 1 to 4 carbon atoms, piperidino and morpholino radicals, 1-piperazinyl radicals (optionally substituted at -4 with an alkyl radical containing 1 to 4 carbon atoms or with a phenylalkyl radical in which

the alkyl part contains 1 to 4 carbon atoms), cycloalkyl radicals containing 3 to 6 carbon atoms, cycloalkenyl radicals containing 4 to 6 carbon atoms, phenyl radicals which are optionally substituted, cyano and carboxyl radicals and alkyloxycarbonyl radicals in which the alkyl part contains 1 to 4 carbon atoms,

- or an aryl radical optionally substituted with one or more atoms or radicals chosen from halogen atoms and alkyl, alkenyl, alkynyl, aryl, aralkyl, alkoxy, alkylthio, aryloxy, arylthio, hydroxyl, hydroxyalkyl, mercapto, formyl, acyl, acylamino, aroylamino, alkoxycarbonylamino, amino, alkylamino, dialkylamino, carboxyl, alkoxycarbonyl, carbamoyl, alkylcarbamoyl, dialkylcarbamoyl, cyano, nitro, azido, trifluoromethyl and trifluoromethoxy radicals, it being understood that R_5 cannot represent a methyl radical or a 4- to 6-membered saturated or unsaturated heterocyclic radical optionally substituted with one or more alkyl radicals containing 1 to 4 carbon atoms,

it being understood that R_5 cannot represent a methyl radical,

it being understood that the cycloalkyl, cycloalkenyl and bicycloalkyl radicals may optionally be substituted with one or more alkyl radicals containing 1 to 4 carbon atoms.

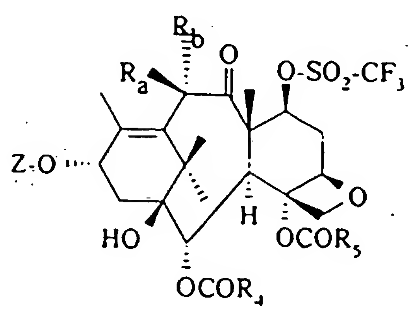
2. Novel taxoids according to claim 1, for which R_a represents a hydroxyl radical, an alkoxy radical containing 1 to 4 carbon atoms, an acyloxy

radical containing 1 to 4 carbon atoms or an alkoxyacetoxy radical in which the alkyl part contains 1 to 4 carbon atoms, and R_b represents a hydrogen atom, Z represents a hydrogen atom or a radical of general formula (II) in which R_1 represents a benzoyl radical or a radical R_2-O-CO- in which R_2 represents a tert-butyl radical, and R_3 represents an alkyl radical containing 1 to 6 carbon atoms, an alkenyl radical containing 2 to 6 carbon atoms, a cycloalkyl radical containing 3 to 6 carbon atoms, a phenyl radical optionally substituted with one or more atoms or radicals, which may be identical or different, chosen from halogen atoms (fluorine or chlorine) and alkyl, alkoxy, dialkylamino, acylamino, alkoxycarbonylamino or trifluoromethyl radicals or a 2- or 3-furyl, 2- or 3-thienyl or 2-, 4- or 5-thiazolyl radical, and R_4 represents a phenyl radical which is optionally substituted with one or more atoms or radicals, which may be identical or different, chosen from halogen atoms and alkyl, alkoxy, amino, alkylamino, dialkylamino, acylamino, alkoxycarbonylamino, azido, trifluoromethyl and trifluoromethoxy radicals, or a 2- or 3-thienyl or 2- or 3-furyl radical, and R_5 represents an optionally substituted alkyl radical containing 1 to 4 carbon atoms, it being understood that R_5 cannot represent a methyl radical.

3. Novel taxoids according to claim 1, for which R_a represents a hydrogen atom or a hydroxyl or

acetyloxy or methoxyacetoxy radical and R_b represents a hydrogen atom, Z represents a hydrogen atom or a radical of the general formula (II) in which R_1 represents a benzoyl radical or a radical R_2-O-CO- in which R_2 represents a tert-butyl radical, and R_3 represents an isobutyl, isobutenyl, butenyl, cyclohexyl, phenyl, 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 2-thiazolyl, 4-thiazolyl or 5-thiazolyl radical, and R_4 represents a phenyl radical which is optionally substituted with a halogen atom, and R_5 represents an alkyl radical containing 2 to 4 carbon atoms.

4. Process for the preparation of a product according to one of claims 1 to 3, characterized in that a product of general formula:



(III)

in which Z, R_4 and R_5 are defined as in one of claims 1 to 3, R_a represents a hydrogen atom or an alkoxy, acyloxy or alkoxyacetoxy radical or a protected hydroxyl radical, and R_b represents a hydrogen atom, is treated with an alkali metal halide or an alkali metal azide or a quaternary ammonium salt or an alkali metal phosphate, optionally followed by replacement of the

protecting group represented by R_a by a hydrogen atom.

5. Process for the preparation of a product according to one of claims 1 to 3, for which R_4 and R_5 are defined as in one of claims 1 to 3, and R_a and R_b each represent a hydrogen atom, characterized in that a product according to one of claims 1 to 3, for which R_a represents a hydroxyl, acyloxy or alkoxyacetoxy radical, is reduced electrolytically.

6. Process for the preparation of a product according to one of claims 1 to 3, for which R_4 and R_5 are defined as in one of claims 1 to 3, and R_a and R_b form, together with the carbon atom to which they are attached, a ketone function, characterized in that a product according to one of claims 1 to 3, for which R_a represents a hydroxyl radical and R_b represents a hydrogen atom, is oxidized.

7. Pharmaceutical composition, characterized in that it contains at least one product according to one of claims 1 to 3, for which Z represents a radical of general formula (II), in combination with one or more pharmaceutically acceptable products, whether inert or pharmacologically active.

VERIFIED TRANSLATION OF PCT

27417/95

IN THE MATTER OF an Australian Application corresponding to PCT Application PCT/FR95/00735

I, Norval O'CONNOR PhD,
c/o Europa House, Marsham Way, Gerrards Cross, Buckinghamshire, England, do solemnly and sincerely declare that I am conversant with the English and French languages and am a competent translator thereof, and that to the best of my knowledge and belief the following is a true and correct translation of the PCT Application filed under No. PCT/FR95/00735.

Date: 11 November 1996

N. O'Connor

N. O'CONNOR
For and on behalf of RWS Translations Ltd.

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